UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

X

UNITED STATES EX REL
INDIVIDUAL A

Plaintiffs,

-Against-

INDIVIDUAL B
INDIVIDUAL C
INDIVIDUAL D
INDIVIDUAL E
INDIVIDUAL F
ENTITY G
JOHN DOs
JANE DOs

Defendants,

X

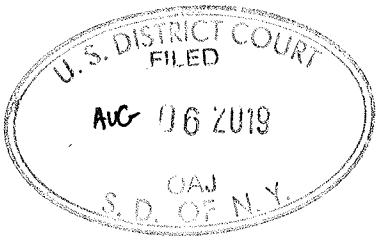
19 CV 7342

COMPLAINT

INDEX NO.

PURSUANT TO
31 U.S.C § 3729

PLAINTIFF
DEMANDS
JURY TRIAL



The Plaintiff alleges the following:

I. SUMMARY OF CASE

This lawsuit is a Qui Tam lawsuit pursuant to the False Claims Act (31 U.S.C. § 3729). On or around February 1, 2010, the Defendants, Hugh C. Hemmings, Jr. and Weill Cornell Medical College submitted for payment and received payment in the amount of $363, 826 with respect to the Research Grant "Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death" under Project Number 5RO1NS056315, from the National Instituted of Health, an Agency of the United States Department of Health and HUman Services. From February 1, 2010 to February 1, 2014, the Defendants, Hugh C. Hemmings, Jr.

and Weill Cornell Medical College submitted for payment and received payment in the amount of ~ $1,431671

In the Grant Application entitled "Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death" under Project Number 5RO1NS056315 which was conceived and written by Dr H.Y. Lim Tung, the Defendants, Hugh C. Hemmings, Jr. and Weill Cornell Medical College stated under penalty of perjury that Dr H.Y. Lim Tung was the Co-Investigator of the Grant Application and an Associate Professor at Weill Cornell Medical College (to be appointed). All the preliminary research data and scientific figures presented in the Grant Application was performed and prepared by Dr H.Y. Lim Tung who is an expert in the areas of Protein Phosphatase-1_I (PP-1_I) purification and characterization and the study of its role in cell death. After the Grant Application obtained a high score and was funded by the NIH, the Defendants, Hugh C. Hemmings, Jr. and Weill Cornell Medical College appropriated the said funded Grant to themselves and did not appoint Dr H.Y. Lim Tung as an Associate Professor and Co-Investigator the said Grant.

From 2010 to 2014, the Defendants, Hugh C. Hemmings, Jr. and Weill Cornell Medical College continuously submitted representations, including Annual Reports that contained false information, stolen data and fabricated data to the NIH that stated that there was nothing wrong with the Grant, presented for payment and collected payment from the NIH ~ $1,431545.

From 2010 and 2014. The Defendants, Hugh C. Hemmings, Jr. and Weill Cornell Medical College who are not experts in the research areas in which the Grant was supposed to fund did not do any significant research work and did not obtain any significant scientific results.

In 2014, out of desperation, the Defendants, Hugh C. Hemmings, Jr., Jumcy Platholi, Paul Heerdt and Weill Cornell Medical College conspired to steal and did steal Dr H.Y. Lim Tung's Scientific Data that Dr H.Y. Lim Tung worked on and prepared in the period 2006 to 2008 and presented the said Scientific Data to the NIH as their own. Further, the Defendants, Hugh C. Hemmings, Jr., Jimcy Platholi, Paul Heerdt and Weill Cornell Medical College conspired to fabricate Data and did fabricate Data, and then submitted via the electronic transmission, the Fabricated Data to the NIH in the form of a Progress Report and in the form of a Scientific Article that contained the Fabricated Data published in the Journal of Biological Chemistry, to mislead and defraud the NIH.

During the period of 2010 to 2014, while the Defendants, Hugh C. Hemmings, Jr., Jumcy Platholi, Paul Heerdt and Weill Cornell Medical College obtained ~ $ 1,431671 from the NIH, the NIH got Stolen Data and Fabricated Data in return. The actions of the Defendants, Hugh C. Hemmings, Jr., Jimcy Platholi, Paul Heerdt and Weill Cornell Medical College constitute Scientific Fraud (pursuant to the definition by the Office of Research Integrity of the United States Department of Health and Human Services), Wire Fraud (18 U.S. Code § 1343) and violated the False Claims Act (31 U.S.C. § 3729).

On or around, the Defendants, Dr Augustine M.K. Choi and Dr Blair and others to be named conspired to hide and did hide the actions of the Defendants, Hugh C. Hemmings, Jr., Jumcy Platholi, Paul Heerdt and Weill Cornell Medical College that constitute Scientific Fraud, Wire Fraud (18 U.S. Code § 1343), and violated the False Claims Act (31 U.S.C. § 3729).

This lawsuit purports to recover the over $ 1,431600 that the Defendants obtained from the NIH under false and fraudulent pretenses. Pursuant to the False Claims Act (31 U.S.C. § 3729), the United States Government is entitled to a return of three times the amount (~$ 4,200000) that the Defendants absconded from the NIH and Dr H.Y. Lim Tung is entitled to between 20% to 30% of the amount recovered from the Defendants. In view of the fact that the Defendants have also committed Scientific Fraud and Wire Fraud, it is also suggested that the US Department of Justice prosecute the Defendants criminally.

II. PARTIES

a. Plaintiff,

2. At all times pertinent, Dr H.Y. Lim Tung was working in the County of New York and residing in the County of Queens.

b. Defendants,

3. The Defendant, Dr Hugh C. Hemmings, Jr. is an Individual who has violated the False Claims Act ((31 U.S.C. § 3729) by submitting for payment and

receiving payment under false pretense from the National Institutes of Health an Agency of the United States Department Health and Human Services. The Defendant, Dr Hugh C. Hemmings, Jr. has also committed Scientific Fraud (Definition of the ORI} and violated the Wire Fraud Statute (18 U.S. Code § 1343).

The address of the Defendant, Dr Hugh C. Hemmings, Jr. is listed as:

Dr Hugh C. Hemmings, Jr.

C/O Weill Cornell Medical College

1300 York Avenue

New York, New York 10065

4. The Defendant, Dr JIMCY PLATHOLI is an Individual who has violated the False Claims Act ((31 U.S.C. § 3729) by submitting for payment and receiving payment under false pretense from the National Institutes of Health an Agency of the United States Department Health and Human Services. The Defendant, Dr Jimcy Platholi has also committed Scientific Fraud (Definition of the ORI} and violated the Wire Fraud Statute (18 U.S. Code § 1343).

The address of the Defendant, Dr Jimcy Platholi is listed as:

Dr Jimcy Platholi

C/O Weill Cornell Medical College

1300 York Avenue

New York, New York 10065

5. The Defendant, Dr Paul Heerdt is an Individual who has violated the False Claims Act ((31 U.S.C. § 3729) by submitting for payment and receiving payment under false pretense from the National Institutes of Health an Agency of the United States Department Health and Human Services. The Defendant, Dr Hugh C. Hemmings, Jr. has also committed Scientific Fraud (Definition of the ORI} and violated the Wire Fraud Statute (18 U.S. Code § 1343).

The address of the Defendant, Dr Paul Heerdt is listed as:

Dr Paul Heerdt

C/O Weill Cornell Medical College

1300 York Avenue

New York, New York 10065

6. The Defendant, Weill Cornell Medical College is an Entity that has violated the False Claims Act ((31 U.S.C. § 3729) by submitting for payment and receiving payment under false and fraudulent pretense from the National Institutes of Health an Agency of the United States Department Health and Human Services. The Defendant, Weill Cornell Medical College. has also committed Scientific Fraud (Definition of the ORI} and violated the Wire Fraud Statute (18 U.S. Code § 1343).

The address of the Defendant, Weill Cornell Medical College is listed as:

Weill Cornell Medical College

1300 York Avenue

New York, New York 10065

7. The Defendant, Dr Augustine C.K. Choi is an Individual who has aided the Defendants, Hugh C. Hemmings, Jr., Jumcy Platholi, Paul Heerdt and Weill Cornell Medical College in violating the False Claims Act ((31 U.S.C. § 3729) through the submission payment demand and receiving payment under false and fraudulent pretense from the National Institutes of Health, an Agency of the United States Department Health and Human Services.

The Defendant, Dr Augustine C.K. Choi has also violated the Wire Fraud Statute (18 U.S. Code § 1343).

The address of the Defendant, Dr Augustine C.K. Choi is listed as:

Dr Augustine C.K. Choi

C/O Weill Cornell Medical College

1300 York Avenue

New York, New York 10065

8. The Defendant, Dr Thomas H. Blair is an Individual who has aided the Defendants, Hugh C. Hemmings, Jr., Jumcy Platholi, Paul Heerdt and Weill Cornell Medical College in violating the False Claims Act (31 U.S.C. § 3729) through the submission payment demand and receiving payment under false and fraudulent pretense from the National Institutes of Health, an Agency of the United States Department Health and Human Services.

The Defendant, Dr Blair has also violated the Wire Fraud Statute (18 U.S. Code § 1343).

The address of the Defendant, Dr Blair is listed as:

Dr Blair

C/O Weill Cornell Medical College

1300 York Avenue

New York, New York 10065

III JURISDICTION AND VENUE

9. Jurisdiction of this lawsuit if founded upon the existence of a federal question arising under the False Claims Act (31 U.S.C. § 3729), Scientific Fraud pursuant to the Office of Research Integrity of the United States Department of Human Health and Human Services and the Wire Fraud Statute (18 U.S. Code § 1343).

10. Venue is founded upon 18 U.S.C. § 1391(1) and 18 U.S.C. § 1391(2) which provide that "venue in civil actions is proper in any of the following: (1) a judicial district in which any defendant resides, if all defendants are residents of the State in which the district is located; (2) a judicial district in which a substantial part of the events or omissions giving rise to the claim occurred, or a substantial part of property that is the subject of the action is situated.

11. The facts and events that underlie this lawsuit took place in large part in the Eastern District of the State of New York .

STATEMENT OF CLAIM

12. This lawsuit is based on the facts as stated below:

13. The facts in this lawsuit were established on records that are stored in the Database of the National Institutes of Health and on records that the Plaintiff Ex Rel possess.

14. On or around February 1, 2010, the Defendants, Hugh C. Hemmings, Jr. and Weill Cornell Medical College submitted for payment to and received payment from the National Institutes of Health, an Agency of the United States Department of Health and Human Services in the amount of $363,826 (EXHIBIT A1).

15. On or around February 1, 2011, the Defendants, Hugh C. Hemmings, Jr. and Weill Cornell Medical College submitted for payment to and received payment from the National Institutes of Health, an Agency of the United States Department of Health and Human Services in the amount of $360,150. (EXHIBIT A2).

16. On or around February 1, 2012, the Defendants, Hugh C. Hemmings, Jr. and Weill Cornell Medical College submitted for payment to and received payment from the National Institutes of Health, an Agency of the United States Department of Health and Human Services in the amount of $360,150. (EXHIBIT A3).

17. On or around February 1, 2013, the Defendants, Hugh C. Hemmings, Jr. and Weill Cornell Medical College submitted for payment to and received payment from the National Institutes of Health, an Agency of the United

States Department of Health and Human Services in the amount of $337,545. (EXHIBIT A4).

18. The payments that the Defendants, Hugh C. Hemmings, Jr. and Weill Cornell Medical College received from the National Institutes of Health, an Agency of the United States Department of Health and Human Services were part of a contract in the form of a Grant Application under Project Number 5RO1NS056315 (EXHIBIT B) termed "Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death" that the Defendants, Hugh C. Hemmings, Jr. and Weill Cornell Medical College had submitted to and solicited from the National Institutes of Health, an Agency of the United States Department of Health and Human Services. In the Said Grant Application.

19. In the said Grant Application, "Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death under Project Number 5RO1NS056315 (EXHIBIT B), the Defendants, Hugh C. Hemmings, Jr. and Weill Cornell Medical College stated under penalty of perjury that Dr H.Y. Lim Tung was the Co-Investigator of the Project and an Associate Professor at Weill Cornell Medical College.

20. Dr H.Y. Lim Tung is the individual who has the expertise to perform the specific aims of the project, "Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death" under Project Number 5RO1NS056315. Dr H.Y. Lim Tung was the individual who initiated the Research Project, performed the experiments and obtained the results that were presented as Preliminary Data in the Grant Application, and wrote the Grant Application. The Specific Aims of the

Research Project call for execution of many Scientific Experiments that if carried out properly and with the right expertise would provide important information on how brain damage occurs following cardiac arrest and resuscitation and also on how to mitigate brain damage following cardiac arrest and resuscitation.

21. Among the important Scientific Experiments that were proposed in the Grant Application, Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death under Project Number 5RO1NS056315 included the Purification and Characterization of an enzyme termed Protein Phosphatase-1_I (PP-1_I) from brain of freshly killed pigs and the study of its regulation at the molecular level. Dr H.Y. Lim Tung is one of few experts in the world who had the knowledge and expertise to purify and characterize PP-1_I holoenzymes from brains of freshly killed pigs or from brains of pigs that had undergone cardiac arrest and resuscitation (EXHIBIT B).

The Defendants, Hugh C. Hemmings, Jr. and Weill Cornell Medical College do not know how, could not and cannot purify PP-1_I holoenzymes from brains of freshly killed pigs or brains of pigs following cardiac arrest and resuscitation.

The Defendants, Hugh C. Hemmings, Jr. and Weill Cornell Medical College do not know how, could not and cannot characterize PP-1_I holoenzymes from brains of freshly killed pigs or brains of pigs following cardiac arrest and resuscitation.

The Defendants, Hugh C. Hemmings, Jr. and Weill Cornell Medical College do not know how, could not and cannot study the role of PP-1_I

holoenzymes in brain damage following cardiac arrest and resuscitation because they do not know how to purify PP-1_I holoenzymes from brains of freshly killed pigs or brains of pigs following cardiac arrest and resuscitation.

The Defendants, Hugh C. Hemmings, Jr. and Weill Cornell Medical College do not know how, could not and cannot study the role of PP-1_I holoenzymes in cell death because they have never performed any cell death studies prior to and after presenting for payment and accepting payment with respect to the NIH funded Research Grant, "Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death" under Project Number 5RO1NS056315.

22. Even though, the Defendants, Hugh C. Hemmings, Jr. and Weill Cornell Medical College stated under penalty of perjury that they would hire Dr H.Y. Lim Tung who is the expert who can perform all the Scientific Experiments proposed and analyze all the results obtained with respect to the funded NIH Research Grant, "Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death" under Project Number 5RO1NS056315, as Co-Investigator and Associate Professor, they did not do so prior to or after presenting for payment and accepting payment with respect to the NIH funded Research Grant, "Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death" under Project Number 5RO1NS056315.

23. The actions of the Defendants, Hugh C. Hemmings, Jr. and Weill Cornell Medical College constitute violation of the False Claim Act (31 U.S.C. § 3729),

24. The actions of the Defendants, Hugh C. Hemmings, Jr. and Weill Cornell Medical College also constitute violation of the Wire Fraud Statute (18 U.S. Code § 1343) because the Defendants, Hugh C. Hemmings, Jr. and Weill Cornell Medical College used electronic transmission to request for payment and received payment that were based on false and fraudulent pretense.

25. In order to request for payment and receive payment with respect to the NIH funded Research Grant Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death under Project Number 5RO1NS056315, the Defendants, Hugh C. Hemmings, Jr. and Weill Cornell Medical College must file via electronic transmission yearly progress reports and affidavit of compliance and regularity. Each year from 2010 to 2015, the Defendants reported that there was nothing wrong with the NIH funded Research, "Grant Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death" under Project Number 5RO1NS056315 and that they were carrying out the Specific Aims of the said NIH funded research grant accordingly.

26. From 2010 to 2014, the Defendants, Hugh C. Hemmings, Jr. and Weill Cornell Medical College hired and used unqualified Scientific Researchers, including the Defendants, Drs Jimcy Platholi and Paul Heerdt to carry out the Specific Aims of the NIH funded Research Grant, Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death (Project Number 5RO1NS056315).

27. Prior to the funding of the NIH funded Research Grant, "Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death" (Project Number

5RO1NS056315), the Defendant, Dr Jimcy Platholi was a student working under the supervision of Dr H.Y. Lim Tung and the Defendant, Dr Jimcy Platholi did not know how, could not and cannot purify PP-1_I holoenzymes from brains of freshly killed pigs or brains of pigs following cardiac arrest and resuscitation.

The Defendant, Dr Jimcy Platholi was afraid of assisting in the operating room when Dr H.Y. Lim Tung was extracting brains from pigs that had or did not have cardiac arrest and resuscitation.

The Defendant, Dr Jimcy Platholi was never involved in the preparation of the brain homogenates from brains of of freshly killed pigs or brains of pigs following cardiac arrest and resuscitation.

The Defendant, Jimcy Platholi did not know how, could not and cannot characterize PP-1_I holoenzymes from brains of freshly killed pigs or brains of pigs following cardiac arrest and resuscitation.

The Defendant, Dr Jimcy Platholi did not know how, could not and cannot study the role of PP-1_I holoenzymes in brain damage following cardiac arrest and resuscitation because they do not know how to purify PP-1_I holoenzymes from brains of freshly killed pigs or brains of pigs following cardiac arrest and resuscitation.

The Defendant, Dr Jimcy Platholi did not know how, could not and cannot study the role of PP-1_I holoenzymes in cell death because she has never performed any cell death studies prior to and after the Research Grant, Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death (Project Number 5RO1NS056315) was funded by the NIH.

27. The Defendant, Paul Heerdt is not an expert who knew or knows how to purify PP-1_I holoenzymes from brains of freshly killed pigs or brains of pigs following cardiac arrest and resuscitation.

The Defendant, Paul Heerdt did not know how, could not and cannot characterize PP-1_I holoenzymes from brains of freshly killed pigs or brains of pigs following cardiac arrest and resuscitation.

The Defendant, Dr Paul Heerdt did not know how, could not and cannot study the role of PP-1_I holoenzymes in brain damage following cardiac arrest and resuscitation because they do not know how to purify PP-1_I holoenzymes from brains of freshly killed pigs or brains of pigs following cardiac arrest and resuscitation.

The Defendant, Dr Paul Heerdt did not know how, could not and cannot study the role of PP-1_I holoenzymes in cell death because he has never performed any cell death studies prior to and after the Research Grant, Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death (Project Number 5RO1NS056315) was funded by the NIH.

Prior to the funding of the Research Grant, Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death (Project Number 5RO1NS056315), the Defendant, Dr Paul Heerdt was assisting Dr H.Y. Lim Tung with physiological studies of pigs following cardiac arrest and resuscitation.

28. on or around February 1, 2014, after four years of submitting for payment and collecting ~ $1,431671 under false and fraudulent pretenses, the Defendants, Drs Hugh C. Hemmings, Jr., Jimcy Platholi, Paul Heerdt and Weill

Cornell Medical College did not have anything concrete to prove that they had carried out the Specific Aims of the NIH funded Research Grant, Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death (Project Number 5RO1NS056315).

29. In order to prove that they were successful in carrying out the Specific Aims of the NIH funded Research Grant, Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death (Project Number 5RO1NS056315), the Defendants, Drs Hugh C. Hemmings, Jr., Jimcy Platholi, Paul Heerdt and Weill Cornell Medical College needed to show that they had published Scientific Results and Scientific Conclusions in peer reviewed Scientific Journals.

30. In their desperation, the Defendants, Drs Hugh C. Hemmings, Jr., Jimcy Platholi, Paul Heerdt and Weill Cornell Medical College stole Scientific Data and Scientific Calculations of Dr H.Y. Lim Tung and claimed them as their own and fabricated Scientific Data and claimed that they were genuine Scientific Data obtained from conducting genuine Scientific Experiments (See EXHIBIT C for details of Stolen Scientific Data and Fabricated Data).

30. Every year from 2010 to 2015, under penalty of perjury and fraud, the Defendants, Drs Hugh C. Hemmings, Jr., Jimcy Platholi, Paul Heerdt and Weill Cornell Medical College submitted Progress Reports via electronic transmission that stated that there was nothing wrong with the NIH funded Research Grant, Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death (Project Number 5RO1NS056315) and progress has been made with respect to achieving the specific aims of the said NIH funded Research Grant

31. The Progress Reports that the Defendants, Drs Hugh C. Hemmings, Jr., Jimcy Platholi, Paul Heerdt and Weill Cornell Medical College submitted to the NIH were false and fraudulent because they contained Fabricated Data and Falsified Data..

32. The Scientific Article entitled "**Regulation of Protein Phosphatase-1, by Cdc25C-associated kinase 1 (C-TAK1) and PFTAIRE Protein Kinase" published in the Journal of Biological Chemistry [J. Biol. Chem (2014) Vol 289, pp23893-23900.]**", published in the Journal of Biological Chemistry that contained Stolen Scientific Data and Fabricated Scientific Data and that the Defendants, Drs Hugh C. Hemmings, Jr., Jimcy Platholi, Paul Heerdt and Weill Cornell Medical College submitted to the NIH on or around January 20, 2015 was the only proof that the Defendants, Drs Hugh C. Hemmings, Jr., Jimcy Platholi, Paul Heerdt and Weill Cornell Medical College had that showed that they had done any Scientific Research Work with respect to the NIH funded Research Grant, Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death (Project Number 5RO1NS056315).

32. From 2010, to 2015, the NIH acted upon the false and fraudulent Progress Reports and continued accepting the Payment Demand from and making the payment to the Defendants, Drs Hugh C. Hemmings, Jr., Jimcy Platholi, Paul Heerdt and Weill Cornell Medical College.

33. On or around February 1, 2015, the Defendants, Drs Hugh C. Hemmings, Jr., Jimcy Platholi, Paul Heerdt and Weill Cornell Medical College.submitted to the NIH, the Scientific Article entitled "Regulation of Protein

Phosphatase-1$_I$ by Cdc25C-associated kinase 1 (C-TAK1) and PFTAIRE Protein Kinase" published in the Journal of Biological Chemistry [J. Biol. Chem (2014) Vol 289, pp23893-23900.] (EXHIBIT D).

The said Scientific Article contained stolen Scientific Data, Scientific Calculations and Scientific Figures that were stolen from Dr H.Y. Lim Tung back in 2008. The said Scientific Article also contained Fabricated Data, Falsified Data and Dishonest Scientific Report (See EXHIBIT E for more details).

34. The NIH did not pay over $ 1,800000 to the Defendants, Drs Hugh C. Hemmings, Jr., Jimcy Platholi, Paul Heerdt and Weill Cornell Medical College.so that they can act to steal Scientific Data, fabricate and falsify Scientific Data, and commit Dishonest Scientific Report.

35. The NIH did not pay over $ 1,800000 to the Defendants, Drs Hugh C. Hemmings, Jr., Jimcy Platholi, Paul Heerdt and Weill Cornell Medical College.so that they can act to publish a Scientific Article entitled " **Regulation of Protein Phosphatase-1$_I$ by Cdc25C-associated kinase 1 (C-TAK1) and PFTAIRE Protein Kinase" published in the Journal of Biological Chemistry [J. Biol. Chem (2014) Vol 289, pp23893-23900.]**", that contained Stolen Scientific Data, Fabricated and Falsified Scientific Data, and Dishonest Scientific Report. (See EXHIBITS D and E for more details).

The actions of the Defendants, Drs Hugh C. Hemmings, Jr., Jimcy Platholi, Paul Heerdt and Weill Cornell Medical College contravene the False Claims Act (31 U.S.C § 3729). Because they use Electronic Transmission to submit Progress Reports that contained false and fraudulent claims to the NIH,

including nonexistent Stolen Scientific Data, Scientific Calculations, Scientific Figures, fictitious Scientific Research Work, Fabricated Data, Falsified Data, Scientific Article that contained stolen Scientific Data, Fabricated Data, Falsified Data and Dishonest Scientific Report, the Defendants, Drs Hugh C. Hemmings, Jr., Jimcy Platholi, Paul Heerdt and Weill Cornell Medical College have also contravened the Wire Fraud Statute (18 U.S. Code § 1343).

36. On or around December 25, 2018, the Defendants, Drs Augustine M.K. Choi and Thomas H. Blair and others to be named prepared a Report under penalty of perjury and fraud that stated that the Defendants, Drs Hugh C. Hemmings, Jr., Jimcy Platholi, Paul Heerdt and Weill Cornell Medical College did not commit any misconduct or fraud with respect to the NIH funded Research Grant, "Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death (Project Number 5RO1NS056315)" and submitted the said Report via electronic submission to the Office of Research Integrity (ORI) of the United States Department of Health and Human Services to hide the actions of the Defendants, Drs Hugh C. Hemmings, Jr., Jimcy Platholi, Paul Heerdt and Weill Cornell Medical College and to not reimburse the NIH over $1,800000 that the Defendants, Drs Hugh C. Hemmings, Jr., Jimcy Platholi, Paul Heerdt and Weill Cornell Medical College obtained from the NIH under false and fraudulent pretense (EXHIBIT F).

37. The actions of the Defendants, Drs Augustine M.K. Choi and Blair and others to be named constitute a violation of the False Claims Act (31 U.S.C § 3729) and the Wire Fraud Statute (18 U.S. Code § 1343).

ALLEGATIONS:

38. The Plaintiff realleges and incorporates by reference herein the allegations set forth in paragraphs as if fully restated hereinafter.

39. The Plaintiff alleges that the Defendants, Drs Hugh C. Hemmings, Jr., Jimcy Platholi, Paul Heerdt, Weill Cornell Medical College, Dr Augustine M.K. Choi and Dr Blair have violated the False Claims Act (31 U.S.C § 3729) and the Wire Fraud Statute (18 U.S. Code § 1343) by:

(i) submitting for payment to and receiving payment from the NIH, an Agency of the United States Department of Health and Human Services under false and fraudulent pretenses and by using electronic transmission to carry out the submission for payment to and the receiving of payment from the NIH under false and fraudulent pretenses.

(ii) submitting false report to the ORI and the NIH to conceal the above'

V. REMEDY AND PRAYER FOR RELIEF

40. The Plaintiff prays that the Honorable Court issue Judgment against the Defendants, Drs Hugh C. Hemmings, Jr., Jimcy Platholi, Paul Heerdt, Weill Cornell Medical College, Dr Augustine M.K. Choi and order them reimburse no less than $6,000000 to the NIH, an Agency of the United States Department of Health and Human Services and to Dr H.Y. Lim Tung pursuant to the False Claims Act [31 U.S.C § 3729 (1)(G)]

41. The Plaintiff also prays that the Honorable Court recommends that the United States Attorney for the Southern District of New York initiate an investigation with respect to the violation of the Wire Fraud Statute (18 U.S. Code § 1343) by the above named Defendants.

Dated: June 20, 2019.

Respectfully Submitted,

DR H.Y. LIM TUNG
PLAINTIFF EX REL
31-70 CRESCENT STREET
ASTORIA, NY 11106

VERIFICATION

HIN Y. LIMTUNG being duly sworn deposes and says that he is the Plaintiff Ex Rel in this proceeding; that he/she has read the annexed Complaint and knows the contents thereof; that the same is true to the knowledge of deponent except as to the matters therein stated to be alleged upon information and belief, and as to those matters he believes it to be true.

Respectfully,

HIN Y. LIMTUNG
31-70 CRESCENT STREET
ASTORIA, NY 11106
TEL: 646-500-1728

SWORN TO BEFORE ME ON THE 20TH ~~DAY OF JUNE~~ 2ND DAY OF AUGUST, 2019

NOTARY PUBLIC

WAI LEONG YUEN
Notary Public, State of New York
Reg. No. 01YU6326204
Qualified in Nassau County
Commission Expires June 15, 2023

STAMP OF NOTARY PUBLIC

EXHIBIT A

Project Information

5R01NS056315-02

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PI PROFILE LINKS

DESCRIPTION RESULTS HISTORY SUBPROJECTS SIMILAR PROJECTS NEARBY PROJECTS BETA LINKS NEWS AND MORE

Project Number: 5R01NS056315-02
Title: ROLE OF PROTEIN PHOSPHATASE-1 IN CEREBRAL ISCHEMIA AND CELL DEATH

Contact PI / Project Leader: HEMMINGS, HUGH C
Awardee Organization: WEILL MEDICAL COLL OF CORNELL UNIV

Contact PI / Project Leader Information:
Name: HEMMINGS, HUGH C
Email: Click to view Contact PI / Project Leader email address
Title: PROFESSOR

Program Official Information:
Name: HICKS, RAMONA R
Email: Click to view PO email address

Other PI Information:
Not Applicable

Profile Exists No Profile

Organization:
Name: WEILL MEDICAL COLL OF CORNELL UNIV
City: NEW YORK **Country:** UNITED STATES (US)

Department Type/ Organization Type:
ANESTHESIOLOGY
SCHOOLS OF MEDICINE

Congressional District:
State Code: NY
District: 12

Other Information:
FOA: PA-07-070
Study Section: Brain Injury and Neurovascular Pathologies Study Section (BINP)
Fiscal Year: 2010 **Award Notice Date:** 22-JAN-2010

DUNS Number: 060217502
Project Start Date: 15-FEB-2009
Budget Start Date: 1-FEB-2010

CFDA Code: 853
Project End Date: 31-JAN-2014
Budget End Date: 31-JAN-2011

Administering Institutes or Centers:
NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

Project Funding Information for 2010:

Total Funding: $363,826

2010	NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE	$363,826

Categorical Spending by IC:

Click here for more information on NIH Categorical Spending

Project Information

5R01NS056315-03

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DESCRIPTION RESULTS HISTORY SUBPROJECTS SIMILAR PROJECTS NEARBY PROJECTS BETA LINKS NEWS AND MORE

Project Number: 5R01NS056315-03
Title: ROLE OF PROTEIN PHOSPHATASE-1 IN CEREBRAL ISCHEMIA AND CELL DEATH

Contact PI / Project Leader: HEMMINGS, HUGH C
Awardee Organization: WEILL MEDICAL COLL OF CORNELL UNIV

Contact PI / Project Leader Information:
Name: HEMMINGS, HUGH C
Email: Click to view Contact PI / Project Leader email address
Title: PROFESSOR

Program Official Information:
Name: HICKS, RAMONA R
Email: Click to view PO email address

Other PI Information: Profile Exists No Profile
Not Applicable

Organization:
Name: WEILL MEDICAL COLL OF CORNELL UNIV
City: NEW YORK **Country:** UNITED STATES (US)

Department Type/ Organization Type:
ANESTHESIOLOGY
SCHOOLS OF MEDICINE

Congressional District:
State Code: NY
District: 12

Other Information:

FOA: PA-07-070
Study Section: Brain Injury and Neurovascular Pathologies Study Section (BINP)
Fiscal Year: 2011 **Award Notice Date:** 12-JAN-2011

DUNS Number: 060217602
Project Start Date: 15-FEB-2009
Budget Start Date: 1-FEB-2011

CFDA Code: 853
Project End Date: 31-JAN-2014
Budget End Date: 31-JAN-2012

Administering Institutes or Centers:

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

Project Funding Information for 2011:

Total Funding: $360,150

2011	NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE	$360,150

Categorical Spending by IC: Click here for more information on NIH Categorical Spending

Text Size A A A

Research Portfolio Online Reporting Tools (RePORT)

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Home > RePORTER > Project Information

RePORT Login | Register | RePORTER Manual System Health: GREEN

Project Information

5R01NS056315-04

Back to Query Form Print Version

PI PROFILE LINKS

DESCRIPTION RESULTS HISTORY SUBPROJECTS SIMILAR PROJECTS NEARBY PROJECTS BETA LINKS NEWS AND MORE

Project Number: 5R01NS056315-04
Title: ROLE OF PROTEIN PHOSPHATASE-1 IN CEREBRAL ISCHEMIA AND CELL DEATH

Contact PI / Project Leader: HEMMINGS, HUGH C
Awardee Organization: WEILL MEDICAL COLL OF CORNELL UNIV

Contact PI / Project Leader Information:

Name: HEMMINGS, HUGH C
Email: Click to view Contact PI / Project Leader email address
Title: PROFESSOR

Program Official Information:

Name: HICKS, RAMONA R
Email: Click to view PO email address

Other PI Information: Profile Exists No Profile

Not Applicable

Organization:

Name: WEILL MEDICAL COLL OF CORNELL UNIV
City: NEW YORK **Country:** UNITED STATES (US)

Department Type/ Organization Type:

ANESTHESIOLOGY
SCHOOLS OF MEDICINE

Congressional District:

State Code: NY
District: 12

Other Information:

FOA: PA-07-070
Study Section: Brain Injury and Neurovascular Pathologies Study Section (BINP)
Fiscal Year: 2012 **Award Notice Date:** 30-JAN-2012

DUNS Number: 060217502
Project Start Date: 15-FEB-2009
Budget Start Date: 1-FEB-2012

CFDA Code: 853
Project End Date: 31-JAN-2014
Budget End Date: 31-JAN-2013

Administering Institutes or Centers:

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

Project Funding Information for 2012:

Total Funding: $360,150

Direct Costs: $214,375

Indirect Costs: $145,775

2012	NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE	$360,150

Categorical Spending by IC:

Click here for more information on NIH Categorical Spending

Download Readers:

Project Information

5R01NS056315-05

Back to Query Form Print Version

PI PROFILE LINKS

DESCRIPTION RESULTS HISTORY SUBPROJECTS SIMILAR PROJECTS NEARBY PROJECTS BETA LINKS NEWS AND MORE

Project Number: 5R01NS056315-05
Title: ROLE OF PROTEIN PHOSPHATASE-1 IN CEREBRAL ISCHEMIA AND CELL DEATH

Contact PI / Project Leader: HEMMINGS, HUGH C
Awardee Organization: WEILL MEDICAL COLL OF CORNELL UNIV

Contact PI / Project Leader Information:
Name: HEMMINGS, HUGH C
Email: Click to view Contact PI / Project Leader email address
Title: PROFESSOR

Program Official Information:
Name: BELLGOWAN, PATRICK S F
Email: Click to view PO email address

Other PI Information:
Not Applicable

Profile Exists No Profile

Organization:
Name: WEILL MEDICAL COLL OF CORNELL UNIV
City: NEW YORK **Country:** UNITED STATES (US)

Department Type/ Organization Type:
ANESTHESIOLOGY
SCHOOLS OF MEDICINE

Congressional District:
State Code: NY
District: 12

Other Information:

FOA: PA-07-070
Study Section: Brain Injury and Neurovascular Pathologies Study Section (BINP)
Fiscal Year: 2013 **Award Notice Date:** 21-FEB-2013

DUNS Number: 060217602
Project Start Date: 15-FEB-2009
Budget Start Date: 1-FEB-2013

CFDA Code: 853
Project End Date: 31-JAN-2015
Budget End Date: 31-JAN-2015

Administering Institutes or Centers:

NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE

Project Funding Information for 2013:

Total Funding: $347,545 **Direct Costs:** $206,872 **Indirect Costs:** $140,673

2013	NATIONAL INSTITUTE OF NEUROLOGICAL DISORDERS AND STROKE	$347,545

Categorical Spending by IC: Click here for more information on NIH Categorical Spending

EXHIBIT B

Project Information

5R01NS056315-05

Project Number: 5R01NS056315-05
Title: ROLE OF PROTEIN PHOSPHATASE-1 IN CEREBRAL ISCHEMIA AND CELL DEATH

Contact PI / Project Leader: HEMMINGS, HUGH C
Awardee Organization: WEILL MEDICAL COLL OF CORNELL UNIV

Abstract Text:

DESCRIPTION (provided by applicant): Global cerebral ischemia due to cardiac arrest results in debilitating neurological impairment necessitating costly long-term health care. Despite this major clinical and economic impact, there is currently no specific medical therapy. Global cerebral ischemia is associated with extensive necrotic and apoptotic cell death; these processes are tightly regulated by several mechanisms, including a critical role for protein phosphorylation. While the involvement of protein kinases in the control of cell death in global cerebral ischemia is well established, the role of protein phosphatases has received relatively little attention. Protein phosphatase-1 is a member of the serine/threonine protein phosphatase subfamily that has been implicated in the regulation of cell death. We have identified and purified several novel multimeric forms of protein phosphatase-1 in mammalian brain. The activity of one of these, termed protein phosphatase-1IC (PP-1IC), is activated in vivo in pig and dog models of global cerebral ischemia as well as in cell culture models of ischemia. Based on these novel findings, we hypothesize that PP-1IC is a component of the signal transduction pathways that link global cerebral ischemia to cell death. In order to determine the mechanisms of activation and the role of PP-1IC in global cerebral ischemia, we propose to purify and characterize the PP-1IC holoenzyme from control and ischemic pig forebrain following cardiac arrest with resuscitation and reperfusion. The molecular compositions of native PP-1IC purified from control and ischemic brain will be determined by mass spectrometry, and the mechanisms of PP-1IC regulation will be studied by reconstitution of the identified components in vitro. Specific membrane permeable inhibitors of PP-1 and other reagents will be developed and used to determine the role of PP-1IC as a mediator of cell death in cell culture models of cerebral ischemia. The mechanisms of ischemic activation of PP-1IC will be investigated based on the hypothesis that the Ca2+regulated protein kinases, Ca2???? dependent protein kinase II (CaMKII) and/or protein kinase C4 (PKC4) function as upstream regulators. These studies will elucidate physiological and pathophysiological mechanisms that regulate native PP-1 holoenzyme activity in brain and define the role of PP-1 in the control of cell death in global cerebral ischemia. This functional proteomics approach is targeted to the development of rational mechanism-based therapies to attenuate ischemic brain cell death, with a long-term goal of clinical translation.

Public Health Relevance Statement:

PUBLIC HEALTH RELEVANCE: Global cerebral ischemia due to cardiac arrest results in debilitating neurological impairment necessitating costly long-term health care. Despite an immense social, medical and economic impact, there is currently no specific pharmacological therapy. The proposed studies will elucidate physiological and pathophysiological mechanisms that regulate native protein phosphatase-1 holoenzymes in brain and determine their role in the control of cell death in global cerebral ischemia. This approach is targeted to the development of rational mechanism-based protein phosphatase-1 inhibitors to attenuate ischemic cell death and neurological injury.

NIH Spending Category:

Biotechnology; Brain Disorders; Neurosciences; Stroke

Project Terms:

Address; Apoptosis; Apoptotic; Attention; Attenuated; base; BCL2 gene; Brain; brain cell; Calcium/calmodulin-dependent protein kinase; calmodulin-dependent protein kinase II; Canis familiaris; Catalytic Domain; Cell Culture Techniques; Cell Death; cell growth regulation; cell injury; Cell physiology; Cell Survival; Cells; Cerebral Ischemia; Cessation of life; Clinical; Co-Immunoprecipitations; Complex; deprivation; design; Development; economic impact; Enzymes; excitotoxicity; Family suidae; Foundations; genetic regulatory protein; Glucose; Glutamate Receptor; Glutamates; Goals; Health; Healthcare; Heart Arrest; Hippocampus (Brain); Holoenzymes; Hour; Hydrogen Peroxide; Impairment; In Vitro; in vivo; inhibitor/antagonist; Ischemia; Lead; Link; Mass Fragmentography; Mass Spectrum Analysis; Mediator of activation protein; Medical; Medical Economics; member; Membrane; Modeling; Molecular; N-Methylaspartate; Na(+)-K(+)-Exchanging ATPase; Necrosis; Nervous System Trauma; neuroblastoma cell; Neurologic; Neurons; Nitric Oxide Synthase; Nitrogen; novel; Oxygen; Pathway interactions; Peptide Hydrolases; Phosphorylation; Physiological; Play; prevent; Process; Property; Prosencephalon; Protein Kinase; Protein Kinase C; Protein phosphatase; Protein Phosphatase Inhibitor; protein phosphatase inhibitor-1; Protein Serine/Threonine Phosphatase; Proteins; Proteomics; Reagent; reconstitution; Regulation; Reperfusion Therapy; Research Proposals; research study; response; Resuscitation; Role; Scaffolding Protein; second messenger; Second Messenger Systems; Shotguns; Signal Pathway; Signal Transduction; Signal Transduction Pathway; Simulate; Site; small molecule; social; Specificity; Spectrometry, Mass, Matrix-Assisted Laser Desorption-Ionization; tandem mass spectrometry; Testing; therapeutic target; Translations; voltage

EXHIBIT C

APPLICATION FOR FEDERAL ASSISTANCE
SF 424 (R&R)

2. DATE SUBMITTED	Applicant Identifier
3. DATE RECEIVED BY STATE	State Application Identifier

1. * TYPE OF SUBMISSION
○ Pre-application ● Application ○ Changed/Corrected Application

4. Federal Identifier
NS056315

5. APPLICANT INFORMATION
* Organizational DUNS:0602175020000
* Legal Name: Joan & Sanford I Weill Medical College of Cornell University
Department: Research & Sponsored Programs
Division: Grants & Contracts
* Street1: 1300 York Avenue
Street2: Box 89
* City: New York
County: New York
* State: NY: New York
Province:
* Country: USA: UNITED STATES
* ZIP / Postal Code: 10065

Person to be contacted on matters involving this application
Prefix: Ms
* First Name: Barbara
Middle Name:
* Last Name: Pfeil
Suffix: JD
* Phone Number: 212-821-0959
Fax Number: 212-821-0799
Email: bip2001@med.cornell.edu

6. * EMPLOYER IDENTIFICATION NUMBER (EIN) or (TIN)
13-1623978

7. * TYPE OF APPLICANT
O: Private Institution of Higher Education

8. * TYPE OF APPLICATION: ○ New ● Resubmission ○ Renewal ○ Continuation ○ Revision

Other (Specify):

Small Business Organization Type
○ Women Owned ○ Socially and Economically Disadvantaged

If Revision, mark appropriate box(es)
○ A. Increase Award ○ B. Decrease Award ○ C. Increase Duration
○ D. Decrease Duration ○ E. Other (specify)

9. * NAME OF FEDERAL AGENCY:
National Institutes of Health

10. CATALOG OF FEDERAL DOMESTIC ASSISTANCE NUMBER:
TITLE:

* Is this application being submitted to other agencies? ○ Yes ● No
What other Agencies?

11. * DESCRIPTIVE TITLE OF APPLICANT'S PROJECT:
Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death

12. * AREAS AFFECTED BY PROJECT *(cities, counties, states, etc.)*
NA

13. PROPOSED PROJECT:
* Start Date: 12/01/2008
* Ending Date: 11/30/2013

14. CONGRESSIONAL DISTRICTS OF:
a. * Applicant: 14
b. * Project: 14

15. PROJECT DIRECTOR/PRINCIPAL INVESTIGATOR CONTACT INFORMATION
Prefix: Dr.
* First Name: Hugh
Middle Name: Carroll
* Last Name: Hemmings
Suffix: Jr.
Position/Title: Professor
* Organization Name: Joan & Sanford I Weill Medical College of Cornell University
Department: Anesthesiology
Division: Research
* Street1: 1300 York Avenue, Room LC-203A
Street2: Box 50
* City: New York
County: New York
* State: NY: New York
Province:
* Country: USA: UNITED STATES
* ZIP / Postal Code: 10065
* Phone Number: 212-746-2714
Fax Number: 212-746-8316
* Email: hchemmi@med.cornell.edu

Project Investigator/Program Director (Last, first, middle): Hemmings, Hugh Carroll

EXHIBIT D(9)

424 R&R and PHS-398 Specific Table Of Contents

EXHIBIT D

424 (R&R) APPLICATION FOR FEDERAL ASSISTANCE

ESTIMATED PROJECT FUNDING

Total Estimated Project Funding	$2,100,000.00
Total Federal & Non-Federal Funds	$2,100,000.00
Estimated Program Income	$0.00

17. * IS APPLICATION SUBJECT TO REVIEW BY STATE EXECUTIVE ORDER 12372 PROCESS?

a. YES — * THIS PREAPPLICATION/APPLICATION WAS MADE AVAILABLE TO THE STATE EXECUTIVE ORDER 12372 PROCESS FOR REVIEW ON DATE

b. NO — PROGRAM IS NOT COVERED BY E.O. 12372 OR

PROGRAM HAS NOT BEEN SELECTED BY STATE FOR REVIEW

By signing this application, I certify (1) to the statements contained in the list of certifications* and (2) that the statements herein are true, complete and accurate to the best of my knowledge. I also provide the required assurances * and agree to comply with any resulting terms if I accept an award. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. (U.S. Code, Title 18, Section 1001)

* I agree

* The list of certifications and assurances, or an internet site where you may obtain this list, is contained in the announcement or agency specific instructions.

*Authorized Representative

* Prefix: Barbara	* First Name:	* Last Name: Filet	Suffix: JD

* Title: Director, Grants & Contracts

* Organization Name: Joan & Sanford I. Weill Medical College of Cornell University

Department: Grants & Contracts

* Street1: 1300 York Avenue

Street2: Box 60

* City: New York

County: New York

* State: NY: New York

* Zip / Postal Code: 10065

Phone Number: 212-821-0560

Fax Number: 212-821-0560

* Email: bfiletti@med.cornell.edu

* Signature of Authorized Representative: Barbara Filet

* Date Signed: 08/13/2008

Pre-application File Name: Name Type:

Attach an additional list of Project Congressional Districts if needed.

Add Name: Name Type:

EXHIBIT D (9).

RESEARCH & RELATED Other Project Information

Are Human Subjects Involved?	Yes / No
If YES to Human Subjects	
Is the IRB review Pending?	Yes / No
IRB Approval Date:	
Exemption Number:	1 2 3 4 5 6
Human Subject Assurance Number	
* Are Vertebrate Animals Used?	Yes / No
* If YES to Vertebrate Animals	
Is the IACUC review Pending?	Yes / No
* IACUC Approval Date:	
Animal Welfare Assurance Number	A3290-01
* Is proprietary/privileged information included in the application?	Yes / No
* Does this project have an actual or potential impact on the environment?	Yes / No
a. If yes, please explain:	
b. If this project has an actual or potential impact on the environment, has an exemption been authorized or an environmental assessment (EA) or environmental impact statement (EIS) been performed?	Yes / No
c. If yes, please explain:	
d. * Does this project involve activities outside the U.S. or partnership with International Collaborators?	Yes / No
e. If yes, identify countries:	
f. Optional Explanation:	
* Project Summary/Abstract	8888-File_15_Abstract.pdf — Mime Type: application/pdf
* Project Narrative	8888-File_16_Narrative.pdf — Mime Type: application/pdf
Bibliography & References Cited	8888-File_17_Bibliography_and_Ref_Cited.pdf — Mime Type: application/pdf
Facilities & Other Resources	1888-File_18_Facilities_and_Other_Res.pdf — Mime Type: application/pdf
Equipment	1818-File_19_Equipment.pdf — Mime Type: application/pdf

Principal Investigator/Program Director (Last, first, middle): Hemmings, Hugh Carroll

EXHIBIT D (3)

Abstract

Global cerebral ischemia due to cardiac arrest results in debilitating neurological impairment necessitating costly long-term health care. Despite this major clinical and economic impact, there is currently no specific medical therapy. Global cerebral ischemia is associated with extensive necrotic and apoptotic cell death. These processes are tightly regulated by several mechanisms, including a critical role for protein phosphorylation. While the involvement of protein kinases in the control of cell death in global cerebral ischemia is well established, the role of protein phosphatases has received relatively little attention. Protein phosphatase-1 is a member of the serine/threonine protein phosphatase subfamily that has been implicated in the regulation of cell death. We have identified and purified several novel multimeric forms of protein phosphatase-1 in mammalian brain. The activity of one of these, termed protein phosphatase-1_{IC} (PP-1_{IC}), is activated *in vivo* in pig and dog models of global cerebral ischemia as well as in cell culture models of ischemia. Based on these novel findings, we hypothesize that PP-1_{IC} is a component of the signal transduction pathways that link global cerebral ischemia to cell death. In order to determine the mechanisms of activation and the role of PP-1_{IC} in global cerebral ischemia, we propose to purify and characterize the PP-1_{IC} holoenzyme from control and ischemic pig forebrain following cardiac arrest with resuscitation and reperfusion. The molecular compositions of native PP-1_{IC} purified from control and ischemic brain will be determined by mass spectrometry, and the mechanisms of PP-1_{IC} regulation will be studied by reconstitution of the identified components *in vitro*. Specific membrane permeable inhibitors of PP-1 and other reagents will be developed and used to determine the role of PP-1_{IC} as a mediator of cell death in cell culture models of cerebral ischemia. The mechanisms of ischemic activation of PP-1_{IC} will be investigated based on the hypothesis that the Ca^{2+}-regulated protein kinases, Ca^{2+}/calmodulin-dependent protein kinase II (CaMKII) and/or protein kinase Cδ (PKCδ) function as upstream regulators. These studies will elucidate physiological and pathophysiological mechanisms that regulate native PP-1 holoenzyme activity in brain and define the role of PP-1 in the control of cell death in global cerebral ischemia. This functional proteomics approach is targeted to the development of rational mechanism-based therapies to attenuate ischemic brain cell death, with a long-term goal of clinical translation.

EXHIBIT C (7)

d Investigator/Program Director (Last, first, middle) Hemmings Hugh Carroll

RESEARCH & RELATED Senior/Key Person Profile (Expanded)

PROFILE - Project Director/Principal Investigator

Prefix	* First Name	Middle Name	* Last Name	Suffix
Dr.	Hugh	Carroll	Hemmings	Jr

Position/Title: Professor

Department: Anesthesiology

Organization Name: Joan & Sanford I Weill Medical College of Cornell Univ-Division: Research

Faculty

* Street1: 1300 York Avenue, Room LC-201A

Street2: Box 99

* City: New York

County: New York

* State: NY: New York

* Country: USA: UNITED STATES

* Zip / Postal Code: 10065

* Phone Number	Fax Number	* E-Mail
212-746-2714	212-746-8310	hehemmi@med.cornell.edu

Credential, e.g., agency login: hehemmi

* Project Role: PDPI

Other Project Role Category:

File Name: 2749-File_6 Biosketch.pdf

Mime Type: application/pdf

* Attach Biographical Sketch

Attach Current & Pending Support

PROFILE - Senior/Key Person

Prefix	* First Name	Middle Name	* Last Name	Suffix
Prefix	MY Lin	Middle Name	Tung	PhD

Position/Title: Associate Professor

Department: Anesthesiology

Organization Name: Joan & Sanford I Weill Medical College of Cornell Univ-Division: Research

Faculty

* Street1: 1300 York Avenue, LC-201

Street2: Box 99

* City: New York

County: New York

* State: NY: New York: Manhattan

* Country: USA: UNITED STATES

* Zip / Postal Code: 10065

* Phone Number	Fax Number	* E-Mail
212-746-8769	212-746-8310	tsungyuanandrewlin@med.cornell.edu

Credential, e.g., agency login

* Project Role: Other (Specify)

Other Project Role Category: Co-Investigator

File Name: UCR-File_6 Biosketch.pdf

Mime Type: application/pdf

* Attach Biographical Sketch

Attach Current & Pending Support

PROFILE - Senior/Key Person

Prefix	* First Name	Middle Name	* Last Name	Suffix
Dr.	Ivan		Lin	PhD

Position/Title: Research Associate

Department: Anesthesiology

Organization Name: Joan & Sanford I Weill Medical College of Cornell Univ-Division: Research

Faculty

* Street1: 1300 York Avenue, Room LC-210

Street2: Box 99

EXHIBIT K(4)

PI: HEMMINGS, HUGH C	Title: Role of Protein Phosphatase-1 in Cerebral Ischemia and Cell Death	
Received: 06/06/2008	FOA: PA07-070	Council: 10/2008
Competition ID: VERSION-2A-FORMS	FOA Title: RESEARCH PROJECT GRANT (PARENT R01)	
1 R01 NS056015-01A2	Dual: AG	Accession Number: 3064311
IPF: 1514809	Organization: WEILL MEDICAL COLLEGE OF CORNELL UNIV	
Former Number:	Department: Anesthesiology	
IRG/SRG: BINP	AIDS: N	Expedited: N
Subtotal Direct Costs (excludes consortium F&A) Year 1: 250,000 Year 2: 250,000 Year 3: 250,000 Year 4: 250,000 Year 5: 250,000	Animals: Y Humans: N Clinical Trial: N Exemption: 10 HESC: N	New Investigator: N

Senior/Key Personnel:	Organization:	Role Category:
Hugh Hemmings Jr.	Joan & Sanford I Weill Medical College of Cornell University	PD/PI
H.Y.Lim Tung PhD	Joan & Sanford I Weill Medical College of Cornell University	Other (Specify)-Co-Investigator
Xiaoli Liu PhD	Joan & Sanford I Weill Medical College of Cornell University	Consultant
Paul Heerdt PhD	Joan & Sanford I Weill Medical College of Cornell University	Consultant
Gary Rakum PhD	University of Maryland school of Medicine	Consultant
Constantino Iadecola MD	Joan & Sanford I Weill Medical College of Cornell University	Consultant

Appendices

File &1b-appendix

Additions for Review

Accepted Publication J Neurochem, 2008 04/30/2008

EXHIBIT B

NIH Modular Budget Backup Information for RASP Office Use

1. Personnel (year 1): If there are changes in personnel in subsequent years, describe in section 6 below.

Name	Role on Project	% Effort	Current Inst. Base Salary	Salary Requested	Fringe Benefit	Total
Hemmings Jr., Hugh, C	Principal Investigator	20%	$ 180,100.00	$ 36,200.00	$ 10,498.00	$46,698.00
Tung, H Y Lan	Co-Investigator	50%	$ 110,000.00	$ 55,000.00	$ 15,950.00	$70,950.00
[illegible], Nandi	Research Associate	100%	$ 45,000.00	$ 45,000.00	$ 12,600.00	$57,600.00
Plaitakis, J	Research Assistant	100%	$ 28,000.00	$ 28,000.00	$7,840.00	$35,840.00
		%	$	$	$	$
		%	$	$	$	$

Use continuation pages if needed.

2. Equipment costs (for items which cost over $2000 and have a life expectancy of at least 2 years):

Year 1: $ 0
Year 2: $ 0
Year 3: $ 0
Year 4: $ 0
Year 5: $ 0
Total: $ 0

3. Patient care costs (not patient research costs): $0.00

4. Alterations and renovations (describe in section 6 below; institutional approval required): $0.00

5. Consortium (subgrant) costs: Attach consortium budget on NIH detailed budget form, accurate to the nearest one thousand dollars. Include indirect costs (F and A) at the consortium institution's approved indirect cost rate. Provide budget for year 1 only and describe significant changes in subsequent years.

Consortium Year 1 Total Direct Costs: $
Consortium Year 1 Indirect Costs [_ % of [ ] S&W or [ ] MTDC]: $
Consortium Year 1 Total Direct Costs plus Indirect Costs: $

Changes in subsequent years:

6. Comments:

Note: All previous Federal Rules and Regulations regarding allowability, allocability, and reasonableness of costs apply to modular budgets. The salary cap of $171,900 per annum is still applicable. Secretarial services and general office supplies cannot be charged to NIH grants, unless specifically requested and justified in the grant application budget justification section.

CORNELL UNIVERSITY

EXHIBIT B(1)

NEW YORK PRESBYTERIAN HOSPITAL

Joan and Sanford I. Weill
Medical College

John J. Savarese, M.D.
The Joseph F. Artusio, Jr. Professor and
Chairman of Anesthesiology
Weill Medical College
Anesthesiologist-in-Chief
New York Presbyterian Hospital

525 East 68th Street
New York NY 10021
Telephone: 212 746-2962
Fax: 212 746-8563
E-mail: jjsavare@med.cornell.edu

September 20, 2005

To Whom It May Concern:

This is to confirm that Dr. H.Y. Lim Tung who currently holds the appointment of Director of the Institute for Neuronal Cell Signaling, Department of Anesthesiology, will be appointed also as Associate Professor in the Department of Anesthesiology, to be effective as of September 1, 2006 thereafter. His salary will be $90,000 per year.

Sincerely,

John J. Savarese, M.D.

JJS/lc

EXHIBIT D

THE JOURNAL OF BIOLOGICAL CHEMISTRY VOL. 289, NO. 34, pp. 23893–23900, August 22, 2014

Regulation of Protein Phosphatase 1_I by Cdc25C-associated Kinase 1 (C-TAK1) and PFTAIRE Protein Kinase*

Received for publication, February 11, 2014, and in revised form, July 6, 2014 Published, JBC Papers in Press, July 15, 2014, DOI 10.1074/jbc.M114.557744

Jimcy Platholi[‡§1], Anna Federman[‡§1], Julia A. Detert[‡], Paul Heerdt[‡§], and Hugh C. Hemmings, Jr.[‡§2]

From the Departments of [‡]Anesthesiology and [§]Pharmacology, Weill Cornell Medical College, New York, New York 10065

Background: Protein phosphatases exist as multisubunit complexes.
Results: Two protein kinases in endogenous brain protein phosphatase 1_I were found to regulate its activation in opposing directions through inhibitor 2 phosphorylation.
Conclusion: These kinases support a signaling cascade that regulates protein phosphatase 1_I activation in global cerebral ischemia.
Significance: Understanding the signaling pathways regulating the activity of protein phosphatases is critical to elucidating their physiological and pathological roles.

Protein phosphatase 1_I (PP-1_I) is a major endogenous form of protein phosphatase 1 (PP-1) that consists of the core catalytic subunit PP-1c and the regulatory subunit inhibitor 2 (I-2). Phosphorylation of the Thr-72 residue of I-2 is required for activation of PP-1_I. We studied the effects of two protein kinases identified previously in purified brain PP-1_I by mass spectrometry, Cdc25C-associated kinase 1 (C-TAK1) and PFTAIRE (PFTK1) kinase, for their ability to regulate PP-1_I. Purified C-TAK1 phosphorylated I-2 in reconstituted PP-1_I (PP-1c·I-2) on Ser-71, which resulted in partial inhibition of its ATP-dependent phosphatase activity and inhibited subsequent phosphorylation of Thr-72 by the exogenous activating kinase GSK-3. In contrast, purified PFTK1 phosphorylated I-2 at Ser-86, a site known to potentiate Thr-72 phosphorylation and activation of PP-1_I phosphatase activity by GSK-3. These findings indicate that brain PP-1_I associates with and is regulated by the associated protein kinases C-TAK1 and PFTK1. Multisite phosphorylation of the I-2 regulatory subunit of PP-1_I leads to activation or inactivation of PP-1_I through bidirectional modulation of Thr-72 phosphorylation, the critical activating residue of I-2.

Protein phosphatase 1 (PP-1)[3] is a ubiquitous multifunctional serine/threonine protein phosphatase. It regulates many neuronal proteins critical to ischemic cell death and protection, including NMDA- and AMPA-type glutamate receptors, voltage-gated Ca^{2+} and Na^+ channels, metabolic enzymes, and components of the apoptotic cell death pathway (1–3). Brain PP-1 exists as hetero-oligomers of the catalytic subunit (PP-1c) associated with targeting proteins, inhibitory regulatory subunits, and/or substrates that confer spatiotemporal and substrate specificity (4, 5). A major form of PP-1 found in the brain is ATP/Mg^{2+}-dependent protein phosphatase 1 (6, 7), also known as protein phosphatase 1_I (PP-1_I). The detailed mechanisms of PP-1_I activation and regulation are currently unclear.

PP-1_I consists of PP-1c and the regulatory subunit inhibitor 2 (I-2) that interact to form an inactive complex (8). Both subunits are expressed ubiquitously in the brain (9, 10). PP-1_I activation is complex and poorly understood. The endogenous kinases that mediate PP-1_I activation and regulation in the brain are unknown, but various protein kinases, including GSK-3, cyclin-dependent kinases, and ERK1, can phosphorylate Thr-72 of I-2 *in vitro* to activate the reconstituted enzyme complex (11, 12). ATP/Mg^{2+}-dependent phosphorylation and activation of PP-1_I is believed to involve relief of inhibition of PP-1c by I-2 via a conformational change in the complex (13).

The identification of endogenous protein kinases that regulate PP-1_I phosphatase activity is critical to understand the role of PP-1 in various signal transduction pathways involved in both physiological and pathological processes. For example, we have shown previously that PP-1_I is activated *in vivo* in a pig model of global cerebral ischemia and reperfusion and that the activated enzyme complex copurifies with two endogenous protein kinases, Cdc25C-associated kinase 1 (C-TAK1) and PFTAIRE kinase (PFTK1) (14). Here we show that these copurifying kinases have opposing actions on PP-1_I activation and therefore may play a role in increasing phosphatase activity following global ischemia and reperfusion.

EXPERIMENTAL PROCEDURES

Materials—ATP, phosphorylase b, tautomycin, bovine serum albumin, and TBB (4,5,6,7-tetrabromobenzotriazole) were from Sigma-Aldrich (St. Louis, MO). Retinoblastoma protein (Rb) was from Millipore (Billerica, MA). D4476 was from Tocris (Bristol, UK). [γ^{32}P]ATP and nickel-nitrilotriacetic acid-Sepharose were from GE Healthcare (Piscataway, NJ). Purified recombinant human GSK-3β and C-TAK1 were from Upstate (Lake Placid, NY), and casein kinase 1 (CK1) and casein kinase 2 (CK2) were from New England Biolabs (Ipswich, MA). Roscovitine, 6-bromoindirubin-3′-oxime, cdk-5, and cdk-5

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[3] The abbreviations used are: PP, protein phosphatase; PP-1c, protein phosphatase 1 catalytic subunit; I-2, inhibitor 2; TBB, 4,5,6,7-tetrabromobenzotriazole; Rb, retinoblastoma protein.

substrate, prepared as described previously (15), were provided by Dr. L. Meijer (Roscoff, France).

Enzymes and Substrates—Native PP-1_I was purified from freshly harvested pig brain as described previously (14). Recombinant human phosphorylase kinase, PP-1c, and I-2 were overexpressed in BL21 (DE3) *Escherichia coli* (Invitrogen) as N-terminal His_6 proteins using the pTrcHis-Topo vector (Invitrogen) and purified by chromatography on nickel-nitrilotriacetic acid-Sepharose. Human PFTK1 was expressed heterologously in HEK cells by transient transfection. The cDNA of full-length human PFTK1 (GenBank™ accession no. AF119833) was inserted into the mammalian expression vector pcDNA3.1(-minus])/Myc-His (Invitrogen) for expression of PFTK1 with a C-terminal myc epitope in HEK 293FT cells (Invitrogen). These cells were grown on 75-cm^2 polycarbonate tissue culture plates in DMEM supplemented with 10% (v/v) fetal bovine serum, 0.1 mM non-essential amino acids, 6 mM L-glutamine, 1 mM sodium pyruvate, 100 units/ml penicillin, 100 μg/ml streptomycin, and 500 μg/ml Geneticin (Invitrogen) at 37 °C in a humidified atmosphere of 95% air and 5% CO_2. Transient transfection of pcDNA3.1(−)/Myc-His-PFTK1 was performed using Lipofectamine 2000 (Invitrogen) according to the instructions of the manufacturer, and transfected 293FT cells were lysed with lysis buffer (50 mM Tris (pH 7.5), 150 mM NaCl, 1 mM EDTA, and complete EDTA-free protease inhibitor mixture (Pierce)). PFTK1 was then immunoprecipitated, and the immune complex was used for kinase assays with purified PP-1_I and I-2 as substrates. Immunoprecipitation was performed using protein G Dynabeads and 5 μg of myc antibody (Invitrogen) or IgG as a control (Pierce).

Preparation of PP-1_I—Native PP-1_I was purified as a holoenzyme from freshly harvested pig rostral brain cytosol as described previously (14). PP-1_I devoid of activating kinase was reconstituted by incubating purified recombinant PP-1c (300 μg) and I-2 (200 μg) in 50 mM imidazole-Cl (pH 7.2), 0.2 mM EGTA, and 0.1% (v/v) 2-mercaptoethanol at 30 °C for 30 min, followed by chromatography through Superdex 200 (16). Fractions with PP-1c or PP-1_I activity, assayed as described in Ref. 12, were pooled and concentrated.

Site-directed Mutagenesis—The full-length human I-2 coding sequence (GenBank™ accession no. NM_006241) was inserted into the pTrcHis vector (Invitrogen) for bacterial expression. Six I-2 mutants (T72A, S86A, S121A, S129A, T184A, and T192A) were generated by PCR using a mutagenesis kit (Stratagene, La Jolla, CA).

Phosphorylation and Phosphatase Assays—[^{32}P]Phosphorylase *a* was prepared by phosphorylation of phosphorylase *b* using phosphorylase kinase. PP-1_I was assayed for its ability to dephosphorylate [^{32}P]phosphorylase *a* following activation by preincubation with ATP/Mg^{2+} as described previously (14). For *in vitro* phosphorylation assays, recombinant I-2 (2 μg) or Rb (2.5 μM) was incubated with 50 mM imidazole (pH 7.4), 0.2 mM EGTA, 0.1% (v/v) 2-mercaptoethanol, 10 mM $MgCl_2$, 100 μM ATP, and 10 μCi [γ-^{32}P]ATP (PerkinElmer Life Sciences) plus C-TAK1 (0.02 μg), GSK-3β (0.02 μg), C-TAK1 and GSK-3β, PFTK1 immunoprecipitate (0.2 mg of Dynabeads/reaction), CK1 (0.2 units/reaction), or CK2 (0.4 units/reaction) and incubated for 1 h at 30 °C. The inhibitors D4476 and TBB were used at 3 μM. Reactions were stopped by addition of 20 μl of SDS-PAGE sample buffer, and proteins were separated by SDS-PAGE and visualized by autoradiography and protein staining (SYPRO or Coomassie Blue, Invitrogen) as described previously (17, 18). Phosphorylation was expressed as a ratio to control band density from autoradiograms and normalized to protein staining. Autoradiograms and gels were scanned on a flatbed gel scanner (Typhoon Trio, GE Healthcare) and analyzed using National Institutes of Health ImageJ software.

Mass Spectrometry—The PP-1_I complex was purified from pig brain, and the individual components were identified by mass spectrometry as described previously (14). For identification of phosphorylation site(s) by mass spectrometry, I-2 phosphorylated by C-TAK1 was separated by SDS-PAGE, stained with Sypro Ruby, excised from the gel, and proteolyzed with trypsin. Then the released tryptic peptides were subjected to phospho-amino acid analysis as described previously (14). Peptides were analyzed by LC electrospray ionization and ion trap MS/MS using an 1100 series LC coupled to an XCT Plus ion trap mass spectrometer (Agilent Technologies, Palo Alto, CA) at the Weill Cornell Medical College Protein Core Facility. Mass spectra were acquired in positive ion mode with automated data-dependent MS/MS on the four most intense ions from precursor MS scans. Analysis of MS/MS spectra was performed by protein database searching with Spectrum Mill bioinformatics software (Agilent Technologies).

Miscellaneous Methods—Protein concentration was determined by the method of Bradford using bovine serum albumin as a standard (19).

Data Analysis—Activity assays and phosphorylation levels included three to four experiments per group. Statistical analyses were performed by two-tailed Student's *t* test or by one-way analysis of variance followed by Tukey's post hoc test for multiple comparisons using GraphPad Prism version 5 software with a threshold for significance set at $p < 0.05$. Data, where applicable, are shown as means ± S.E. or S.D. as indicated. Asterisks indicate values significantly different from control groups: *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$.

RESULTS

Activation of PP-1_I—PP-1_I purified from fresh pig brain was used to identify endogenous components of the PP-1_I complex and their regulation of phosphorylase *a* phosphatase activity. Purified PP-1_I was activated markedly by preincubation with ATP/Mg^{2+} (Fig. 1*A*), indicating the presence of a copurifying PP-1_I-activating kinase. Specific inhibitors of GSK-3 (6-bromoindirubin-3′-oxime, IC_{50} of 5 nM) or cdk-5 (roscovitine, IC_{50} of 200 nM), exogenous kinases known to phosphorylate and activate I-2 *in vitro* (11, 12), did not inhibit the activation of purified brain PP-1_I by ATP/Mg^{2+} (data not shown). Therefore, we focused our attention on the ability of two protein kinases shown previously to copurify with brain PP-1_I (14) to regulate PP-1_I.

In addition to the core catalytic subunit PP-1c and the regulatory subunit I-2, purified brain PP-1_I contains four major additional proteins, including the two kinases C-TAK1 (81 kDa) and PFTK1 (52 kDa) (Fig. 1, *B* and *C*) (14). C-TAK1 is a component of the MAP kinase scaffolding complex and has

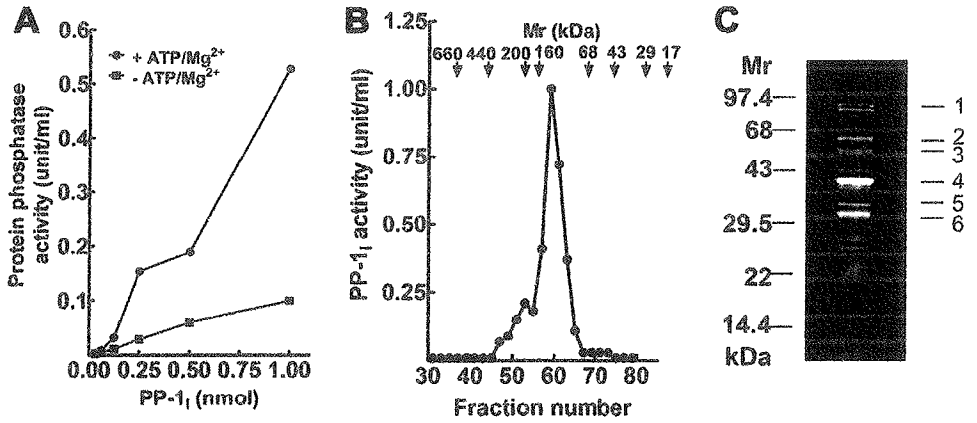

FIGURE 1. **ATP-dependent activation of native PP-1_I.** *A*, native PP-1_I purified 1120-fold from pig brain (14) was incubated without (■) or with (●) ATP/Mg^{2+} for 5 min prior to initiation of the phosphatase assay by the addition of [^{32}P]phosphorylase *a*. Incubation with ATP/Mg^{2+} increased phosphatase activity ~5-fold. *B*, chromatography of purified PP-1_I on Superdex 200 showing elution at M_r ~160,000. PP-1_I was assayed using [^{32}P]phosphorylase *a* as a substrate following preincubation with ATP/Mg^{2+} and GSK-3β. *C*, SDS/PAGE analysis of brain PP-1_I showing copurification of six major proteins (n = 3).

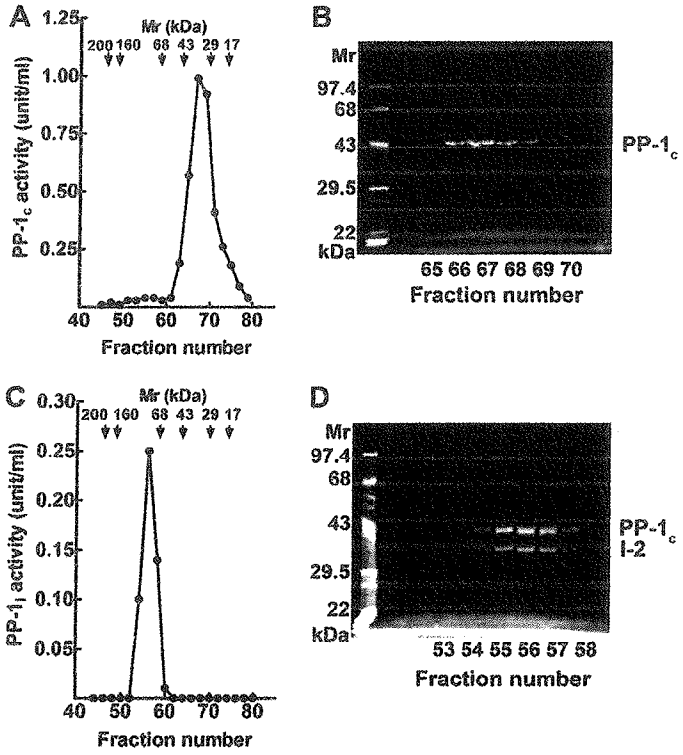

FIGURE 2. **Reconstitution of core PP-1_I from purified recombinant PP-1c and I-2.** *A*, chromatography of recombinant PP-1α_{cat} on Superdex 200 showing elution at M_r 40. PP-1 activity was assayed using [^{32}P]phosphorylase *a* as a substrate. *B*, SDS/PAGE analysis of PP-1c eluted from Superdex 200. *C*, chromatography of reconstituted PP-1_I on Superdex 200 showing elution at M_r 75. PP-1_I was assayed using [^{32}P]phosphorylase *a* as a substrate following preincubation with ATP/Mg^{2+} and GSK-3β. *D*, SDS/PAGE analysis of reconstituted PP-1_I eluted from Superdex 200 showing coelution of PP-1c and I-2 at M_r ~70,000 (n = 3).

been identified as a kinase phosphorylating Cdc25, consistent with its ubiquitous expression in the brain (20–22). Similarly, PFTK1 is a cdc2-related kinase highly expressed in the brain (23, 24).

Regulation of Reconstituted PP-1$_I$ by C-TAK1 and PFTK1—To determine the effects of these kinases on PP-1_I activity, PP-1_I devoid of activating kinase was reconstituted from purified recombinant PP-1c and I-2 (Fig. 2, *A–D*). The reconstituted PP-1_I eluted with an apparent molecular mass of 70 kDa by gel filtration (Fig. 2*C*). C-TAK1 and immunoprecipitated PFTK1 phosphorylated I-2 (Fig. 3*A*). However, neither C-TAK1 nor PFTK1 directly activated reconstituted PP-1_I, whereas it was activated by preincubation with the positive control kinase GSK-3β (Fig. 3, *B* and *C*). Interestingly, prior phosphorylation of reconstituted PP-1_I by C-TAK1 significantly reduced subsequent activation by GSK-3β (Fig. 3*B*), indicating that C-TAK1 acts as an inhibitory kinase. Taken together, these results indicate that neither of the copurifying kinases, C-TAK1 and PFTK1, is an endogenous activating kinase. Therefore, these kinases likely phosphorylate I-2 on residues distinct from Thr-72.

Identification of the C-TAK1 Phosphorylation Site—The phosphorylated tryptic peptide fragment corresponding to amino acid residues IDEPSTPYHSMMGDDEDACSDTEATEAMAPDILAR plus a phosphoryl group (m/z = 1313.5^{3+}) was identified in I-2 phosphorylated by C-TAK1. Analysis of the MS/MS spectra of the phospho-I-2 fragmentation pattern showed the presence of two subfragments (y_{27}^{2+}, m/z = 1477.7; y_{32}^{2+}, m/z = 1790.1) corresponding to HSMMGDDEDACSDTEATEAMAPDILAR and p(STPY)HSMMGDDEDACSDTEATEAMAPDILAR, respectively, indicating that the site of phosphorylation is localized within STPY (Fig. 4). Phospho-amino acid analysis of I-2 phosphorylated by C-TAK1 identified only phosphoserine (data not shown). Therefore, the site in I-2 phosphorylated by C-TAK1 is Ser-71. Because C-TAK1 reduced subsequent activation by GSK-3β (Fig. 3*B*) of reconstituted PP-1_I, we tested whether this corresponded to phosphorylation of I-2 Thr-72. Phosphorylation of I-2 by C-TAK1 at Ser-71 reduced subsequent phosphorylation of Thr-72 by GSK-3 (Fig. 5). These results indicate that C-TAK1 functions as an inhibitory protein kinase by phosphorylating an adjacent residue, therefore reducing PP-1_I activation via Thr-72 phosphorylation.

Identification of the PFTK1 Phosphorylation Site—Phosphorylation of I-2 by isolated PFTK1 occurred at low stoichiometry (Fig. 6*A*). Therefore, serial alanine scanning mutagenesis was necessary to determine the site of I-2 phosphorylated by PFTK1. A NetPhosK 1.0 search with a threshold of 0.45 identified 13 putative sites for phosphorylation by CDKs among the

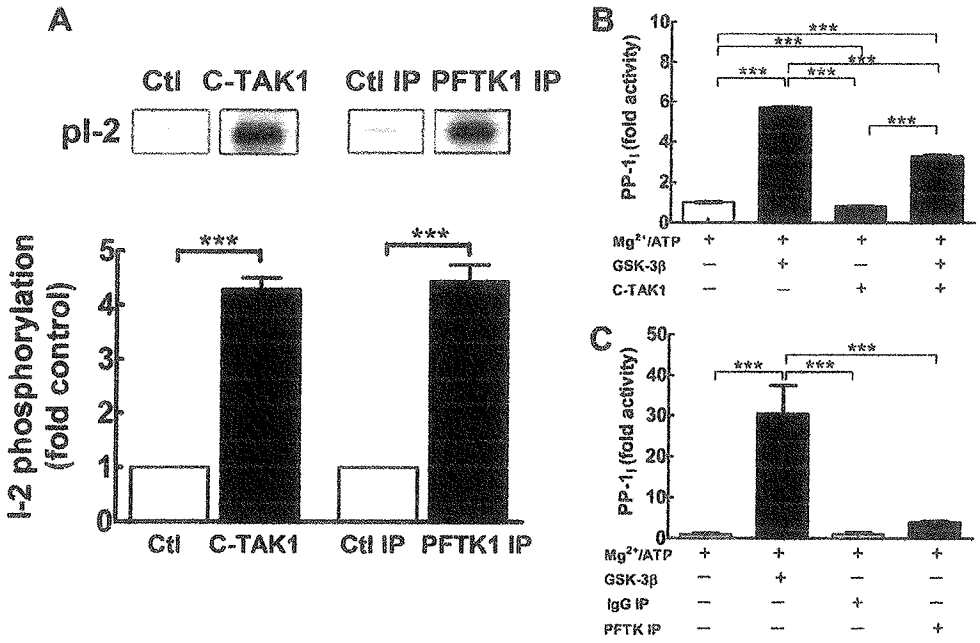

FIGURE 3. **Reconstituted PP-1$_1$ is not activated by C-TAK1 or PFTK1.** Recombinant I-2 was incubated with Mg^{2-}/[γ-^{32}P]ATP (control (*Ctl*) and control IgG immunoprecipitate (*Ctl IP*)) or with Mg^{2+}/[γ-^{32}P]ATP plus C-TAK1 (*C-TAK1*) or PFTK1 (*PFTK1 IP*), all including 100 nM tautomycin, for 30 min at 30 °C. Reactants were separated by SDS/PAGE, and the gels were stained, destained, dried, and subjected to autoradiography. Representative autoradiogram (*A*, *top panel*) and quantitative densitometric analysis (*A*, *bottom panel*) of I-2 phosphorylation (*pI-2*) (relative to background phosphorylation by control or IgG immunoprecipitate) are shown. Data are mean ± S.E. ($n = 3$). ***, $p < 0.001$ *versus* control (Student's *t* test). *B*, reconstituted PP-1$_1$ (0.2 μg) assayed in the presence of Mg^{2+}/ATP alone (*Ctl*) or Mg^{2-}/ATP plus GSK-3β (0.01 μg), C-TAK1 (0.02 μg), or GSK-3β and C-TAK1. *C*, reconstituted PP-1$_1$ (0.2 μg) assayed for phosphatase activity in the presence of Mg^{2+}/ATP (control), Mg^{2+}/ATP plus IgG IP (control), Mg^{2+}/ATP plus GSK-3 β (0.01 μg), or PFTK1 immunoprecipitate. C-TAK1 or PFTK1 did not activate reconstituted PP-1$_1$. However, prior phosphorylation of I-2 by C-TAK1 reduced subsequent activation of PP-1$_1$ by GSK-3 β (B). Data are mean ± S.E. ($n = 3$). ***, $p < 0.001$ *versus* control (one-way analysis of variance).

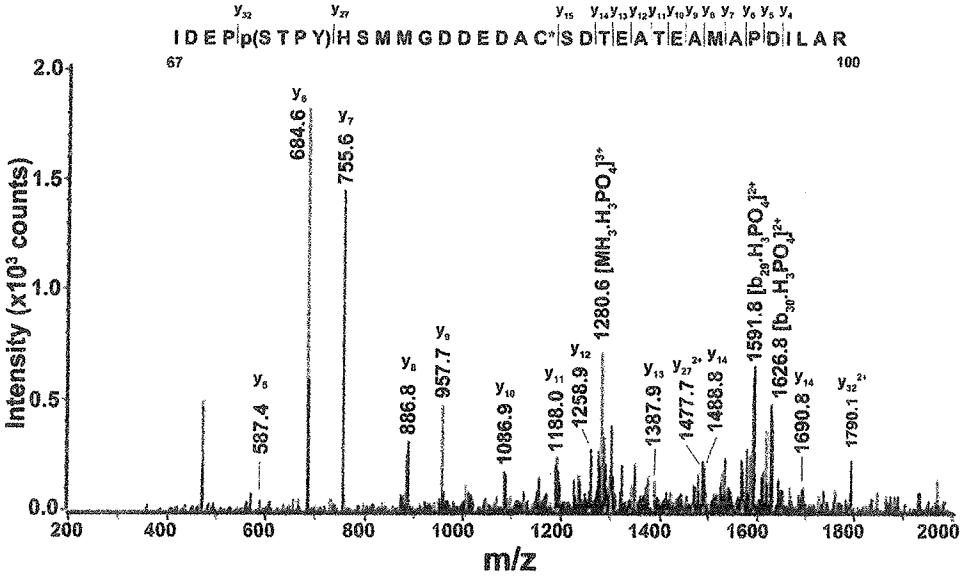

FIGURE 4. **MS/MS spectra of the tryptic phosphopeptide from I-2 phosphorylated by C-TAK1.** I-2 was phosphorylated with C-TAK1, subjected to SDS/PAGE, excised, and digested with trypsin. Liberated peptides were then analyzed by LC electrospray ionization MS/MS. MS/MS spectra of a phosphopeptide ($m/z = 1313.5^{3+}$) were obtained and analyzed. b and y ions are marked in the spectra. The amino acid sequence of the phosphopeptide is shown at the *top*. Subfragment ion y_{27}^{2+} (p(STPY) HSMMGDDEDACSDTEATEAMAPDILAR, $m/z = 1790.1$) was identified in the phosphopeptide preparation, indicating that the site phosphorylated by C-TAK1 is within STPY. The phosphorylated residue was confirmed as Ser-71 by phospho-amino acid analysis. C*, acrylamide-modified cysteine.

33 Ser/Thr residues in the 204-amino acid human I-2 sequence (25). Six possible sites were selected for further evaluation as potential PFTK1 phosphorylation sites by site-directed mutagenesis on the basis of NetPhosK high predictive scores (Thr-72, Ser-121, Ser-129, Thr-184, and Thr-192) or prior identification as I-2 phosphorylation sites in the Protein Knowledge Base (Ser-86, Thr-72, and Ser-121; UniProtKB IPP2_HUMAN P41236). Of the six residues selected, there was no significant difference in phosphorylation by PFTK1 upon mutation of five sites (Thr-72, Ser-121, Ser-129, Thr-184, and Thr-192) to alanine, indicating that these are not PFTK1 phosphorylation sites (Fig. 6*B*). However, the S86A mutation

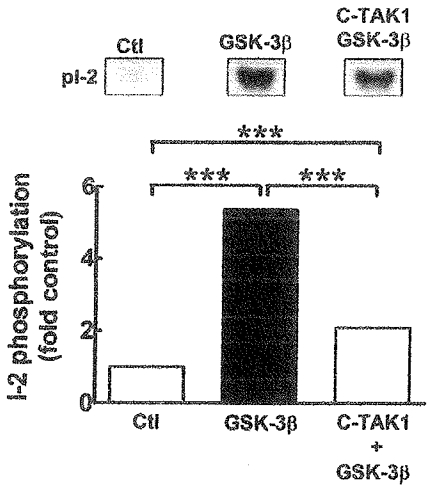

FIGURE 5. **Phosphorylation of I-2 by C-TAK1 inhibits subsequent phosphorylation by GSK-3β.** I-2 (2 μg) was incubated with Mg^{2+}/[γ-^{32}P]ATP (control (*Ctl*), *top left panel*), Mg^{2+}/[γ-^{32}P]ATP plus GSK-3β (0.02 μg) (*top center panel*), or Mg^{2+}/ATP plus C-TAK1 (0.02 μg) for 30 min and then with Mg^{2+}/[γ-^{32}P]ATP plus GSK-3β (0.02 μg) (*top right panel*). Reactants were separated by SDS/PAGE, and the gels were stained with Coomassie Blue, destained, dried, and subjected to autoradiography (*top panels*) and quantitative analysis (*bottom panel*). Prior phosphorylation of I-2 by C-TAK1 reduced subsequent phosphorylation by GSK-3β. Data are mean ± S.E. ($n = 3$). ***, $p < 0.001$ *versus* control (one-way analysis of variance).

reduced I-2 phosphorylation by PFTK1 by 58 ± 2.5% compared with wild-type I-2, establishing this as a major site of phosphorylation by PFTK1 (Fig. 6*C*, *left*). In agreement with our finding that Thr-72 is not a PFTK1 phosphorylation site, PFTK1 did not activate reconstituted PP-1_1 (Fig. 3*C*). The PFTK1 phosphorylation site Ser-86 is also phosphorylated by either CK1 or CK2 (26–29). To rule out Ser-86 phosphorylation by contaminating CK1 or CK2 in the immunoprecipitated PFTK1 preparation, the CK1 inhibitor D4476 (30) or the CK2 inhibitor TBB (31) was included in kinase assays. The S86A mutation decreased phosphorylation of I-2 by both purified CK1 and CK2 as expected (Fig. 6*C*, *center* and *right*). D4476 (3 μM) significantly inhibited I-2 phosphorylation by CK1 but did not affect phosphorylation of I-2 by PFTK1 (Fig. 6*D*). Similarly, TBB (3 μM) significantly inhibited I-2 phosphorylation by CK2 but did not affect phosphorylation of I-2 by PFTK1 (Fig. 6*D*). Therefore, phosphorylation of I-2 by PFTK1 was not due to contamination of the PFTK1 immunoprecipitate with CK1 or CK2. Furthermore, although both CK1 and CK2 were present in HEK 293FT cell lysate, they were not detected in the PFTK1 immunoprecipitate by immunoblotting (data not shown). Together, these results indicate that PFTK1 phosphorylates I-2 at Ser-86. Phosphorylation of I-2 Ser-86 by CK2 has been shown previously to poten-

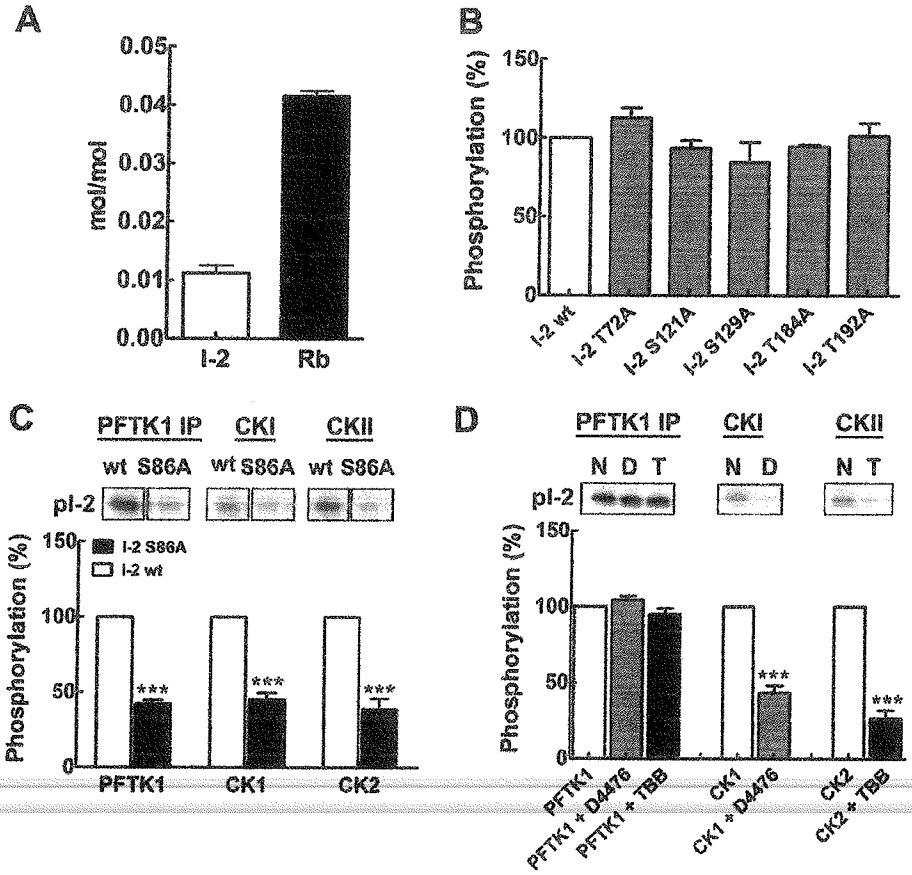

FIGURE 6. **PFTK1 phosphorylates I-2 at Ser-86.** *A*, stoichiometry of the phosphorylation of I-2 and Rb (positive control) by PFTK1. PFTK1 phosphorylated I-2 to one-fourth the stoichiometry of Rb phosphorylation. Data are mean ± S.E. ($n = 3$). *B*, recombinant I-2 WT and five Ser/Thr → Ala mutants were incubated with Mg^{2+}/[γ-^{32}P]ATP and PFTK1 for 1 h at 30 °C. The I-2 reactants were separated by SDS/PAGE, and the gels were stained with Sypro protein stain and subjected to autoradiography. Phosphorylation was calculated as a percentage of WT band density from autoradiograms and normalized to Sypro protein staining. Densitometric analysis of I-2 WT and mutant phosphorylation by PFTK1 are shown. Data are mean ± S.E. ($n = 2$). *C*, representative autoradiograms (*top panel*) and quantitative densitometric analysis (*bottom panel*) from *in vitro* phosphorylation assays of I-2 WT and S86A mutant I-2 phosphorylated by PFTK1, CK1, or CK2. *IP*, immunoprecipitate. *D*, phosphorylation of I-2 WT by PFTK1, CK1, or CK2 in the presence of the CK1 inhibitor D4476 (*D*) or the CK2 inhibitor TBB (*T*). *N*, no inhibitor. Data are mean ± S.E. ($n = 4$). ***, $p < 0.001$ *versus* WT or without inhibitor (Student's *t* test).

tiate activation of PP-1_I by the activating kinase GSK-3β (26, 29). On the basis of these studies, PFTK1 should activate PP-1_I indirectly by facilitating Thr-72 phosphorylation. However, because *in vitro* phosphorylation studies are limited, we cannot rule out that minor sites other than Ser-86 also contribute functionally to PP-1_I modulation by PFTK1.

DISCUSSION

Native PP-1_I isolated from fresh pig brain consists of the catalytic subunit PP-1c, the inhibitory regulatory protein I-2, and several potential regulatory proteins. To preserve the integrity of the native PP-1_I complex, it must be purified from the brain immediately following death because of rapid post-mortem loss of activity (Ref. 14 and data not shown). The finding that purified PP-1_I is activated by incubation with ATP/Mg^{2+} indicates the presence of a copurifying activating kinase. Six major proteins have been identified in purified PP-1_I, two of which are protein kinases (14). Here we report that the two copurifying kinases, C-TAK1 and PFTK1, phosphorylate I-2 at sites that can modulate phosphorylation of the activating residue Thr-72. This is consistent with a role for this multisite phosphorylation in the regulation of endogenous brain PP-1_I in global cerebral ischemia.

Neither of the protein kinases identified by proteomic analysis of purified brain PP-1_I phosphorylated I-2 at Thr-72 or activated reconstituted PP-1_I. Because reconstituted PP-1_I was activatable by GSK-3β, the activating kinase must be present in the native complex at a lower molar ratio, or the complex is so labile that it was not detected in our proteomic analysis (14). Future studies involving alternative approaches to analyzing the PP-1_I holoenzyme will be required to identify the endogenous copurifying kinase.

The activating kinase for brain PP-1_I has been proposed to be GSK-3 (6). However, the endogenous activating kinase present in purified pig brain PP-1_I is not GSK-3 because the specific GSK-3 inhibitor 6-bromoindirubin-3′-oxime did not prevent PP-1_I activation. This is supported by an analysis of Thr-72 phosphorylation in HeLa cells in which the kinase appeared to be a cyclin-dependent kinase (32). However, the specific cdk-5 inhibitor roscovitine also did not prevent PP-1_I activation. MAP kinase has been implicated in growth factor-induced activation of PP-1_I (12), but has not been implicated as the activating kinase in brain, and was not identified in the PP-1_I complex by mass spectrometry.

The two protein kinases that copurify with PP-1_I, C-TAK1 and PFTK1 (14), had opposing effects on the modulation of PP-1_I activity. C-TAK1 acts as an inhibitory kinase by phosphorylating I-2 at a novel site (Ser-71) to reduce subsequent phosphorylation of the adjacent Thr-72, probably through steric and electrostatic hindrance by the phosphoryl group. In contrast, PFTK1 phosphorylates I-2 at Ser-86, a site known to potentiate PP-1_I activation (26, 29). Therefore, the PP-1_I complex includes kinases capable of bidirectional modulation of PP-1_I activity through phosphorylation of the regulatory subunit I-2. A role for these sites in PP-1_I regulation is consistent with the previous finding that endogenous I-2 is phosphorylated on at least one residue other than Thr-72 between residues 70 and 90 by a kinase other than GSK-3 (28). On the basis of the expression of PP-1_I and its regulatory components in the brain and their copurification in brain PP-1_I, both kinases could play a role in regulating endogenous PP-1_I activity. In the basal state, C-TAK1 phosphorylation of Ser-71 would keep PP-1_I activity low. Activation of PFTK1, possibly through a cyclin pathway (23), leading to phosphorylation of Ser-86 would increase PP-1_I activity.

Endogenous PP-1_I activation is complex and has not been verified in *in vivo* studies. *In vitro* studies show that phosphorylation of Thr-72 on I-2 converts PP1c to its active conformation. When active, PP1c dephosphorylates I-2 before it can dephosphorylate exogenous substrates (33–38). This complex activation mechanism is highly conserved across species (39, 40), suggesting a physiological role. The presence of PP1c and I-2 in our purified holoenzyme and the necessity for Mg^{2+}/ATP for activation indicates that endogenous PP-1_I is most likely regulated in a similar manner. However, it is important to point out that direct evidence for phosphorylation of Thr-72 of I-2 *in vivo* is limited. Analysis of rabbit skeletal muscle I-2 by fast atom bombardment mass spectrometry revealed only serine phosphorylation (41). This has been corroborated by immunoprecipitation of I-2 extracts also showing that 90–95% of phosphorylation was on seryl residues (42). This is consistent with the transient nature of Thr-72 phosphorylation in the mechanism of PP-1_I activation.

Previous work has implicated PP-1 in the pathobiochemistry of cerebral ischemia. For example, we have shown previously that PP-1_I activity increases following global cerebral ischemia/reperfusion *in vivo* (14). Moreover, PP-1 controls critical neuroprotective and cell death pathways in the brain (43). In PP-1_I purified from control and ischemic brain, the amounts of C-TAK1 and PFTK1 were decreased or increased, respectively (14). This is consistent with multisite phosphorylation changes in I-2 leading to increased PP-1_I activation following global cerebral ischemia. Because C-TAK1 inhibits PP-1_I activation, although PFTK1 facilitates PP-1_I activation, these kinases could contribute to a signaling cascade that results in increased PP-1_I activity following global cerebral ischemia.

PP-1c interacts with and dephosphorylates critical components of the apoptotic cell death pathway, including Rb, Bcl-2, Bcl-X_L, Bcl-w, and Bad, implicating PP-1 in the control of cell death (44, 45). 14-3-3 prevents Bad, an essential proapoptotic factor, from binding to and inactivating the antiapoptotic factor Bcl-X_L in a phosphorylation-dependent manner. The finding that 14-3-3 interacts with purified (14) and reconstituted PP-1_I provides a mechanism for targeting of PP-1_I to cell death effectors (14) and implicates PP-1_I in the dephosphorylation of Bad, a key step in the initiation of apoptosis. C-TAK1 is a ubiquitously expressed serine/threonine kinase involved in various cellular functions through generation of 14-3-3 binding sites (46). Therefore, in addition to inhibition of PP-1_I phosphatase activity through Ser-71 phosphorylation, a mechanism involving PP-1_I, 14-3-3, and C-TAK1 could also regulate activation of PP-1_I in ischemia. Phosphorylation of I-2 Ser-86 could be an important positive regulatory step involved in the synergistic activation of PP-1_I by PFTK1 and an activating kinase. The resulting increase in PP-1 activity would activate apoptosis following global cerebral ischemia through dephosphorylation of

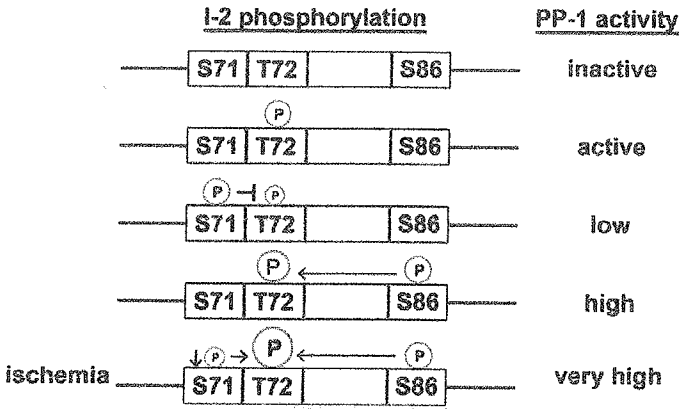

FIGURE 7. **Schematic models of PP-1_I activation relative to I-2 phosphorylation.** I-2 inhibition (*inactive*) of PP-1c is relieved when Thr-72 of I-2 is phosphorylated (*active*). Prior phosphorylation of Ser-71 reduces phosphorylation of Thr-72 (*low*) and, therefore, reduces PP-1_I activity. In contrast, prior phosphorylation of Ser-86 results in increased phosphorylation of Thr-72 (*high*) and, therefore, increases PP-1_I activity. Under ischemic conditions, with increased PFTK1 activity and reduced CTAK1 activity, both of these phosphorylation events would lead to enhanced phosphorylation of I-2 Thr-72 (*ischemia*) and PP-1_I activity (*very high*). Stoichiometry of phosphorylation is proportional to symbol size.

cell death regulators such as Bad and Rb (45, 47) (Fig. 7). Further studies are warranted to address the role of these kinases in the regulation of PP-1_I activity following global cerebral ischemia.

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EXHIBIT E

A. Evidence of Data Fabrication, Data Falsification, Dishonest Scientific Report, Theft of Idea and Theft of Data in the Scientifc Article "Regulation of Protein Phosphatase-1I by Cdc25C-associated kinase 1 (C-TAK1) and PFTAIRE Protein Kinase" in the Journal of Biological Chemistry [J. Biol. Chem (2014) Vol 289, pp23893-23900.]

A major proportion of the experiments and results described in the scientific article were performed, analyzed and calculated by myself in 2006 to 2008. The other half were supposedly performed by them after I was forced to leave Weill Cornell Medical College and consisted of Fabricated Data and Falsified Data. In the scientific article, Hugh C. Hemmings, Jr. and Jimcy Platholi thanked me for contributions and for Mass Spectrometry Analysis without my knowledge and permission. [They did not have the decency to ask me for my permission to use my name in the Scientific Article]. I did not initiate the research, perform the experiments, analyze the data, made the calculations, prepare the Figures to be thanked in the Acknowledgment Section.

I am the person who purified the PP-1I holoenzyme. I challenged Hugh C. Hemmings, Jr. and Jimcy Platholi to purify PP-1I holoenzyme from pig brain (freshly killed) from start to finish by themselves in the laboratory. The reason that they published only one Scientific Article (half of the work described in the paper was performed by me and the other half consists of Fabricated Data and Falsified Data) from 2009 to 2014 with funding of over $2,100000 is because they do not know how to purify PP-1I holoenzyme from pig brain, They would not even know how to extract the brain from a live animal let alone prepare a homogenate of pig brain. That is how incompetent they are.

Theft of Data:

A. In the paper, the authors including Hugh C. Hemmings, Jr. and Jimcy Platholi stated in the Method Section that Protein Phosphatase-1I (PP-1I) was purified as described in the scientific article , giving the impression that they themselves performed the purification which is far from the truth. Figure 1 shows a picture of the SDS PAGE

pattern of PP-1I that was purified by myself in 2006. The picture was taken in 2006. Hugh C. Hemmings, Jr. and Jimcy Platholi could not and did not purify PP-1I in 2006. Hugh C. Hemmings, Jr. had abandoned the laboratory long before 2006 and Jimcy Platholi was a Ph.D. student working under my supervision in 2006. Jimcy Platholi was afraid of being in the Operating Room when I was extracting brain tissue from a freshly killed pig. Jimcy Platholi was also absent when I was homogenizing the brain tissue and purifying PP-1I from the brain homogenate in the cold room and when I was purifying PP-1I through various chromatographic steps.

B. In the paper, the authors including Hugh C. Hemmings, Jr. and Jimcy Platholi stated in the Method Section that ^{32}P-labeled phosphorylase a was prepared as described in the method article , giving the impression that they themselves performed the preparation of ^{32}P-labeled phosphorylase a which is far from the truth. ^{32}P-labeled phosphorylase a described in the paper was prepared by myself in 2006.

C. In the paper, the authors including Hugh C. Hemmings, Jr. and Jimcy Platholi showed the picture of the MS/MS spectra of the tryptic phosphopeptide from I-2 phosphorylated by C-TAK-1. The authors imply that they made the discovery that I-2 is phosphorylated by C-TAK-1 on Serine 71 which is far from the truth. The authors also stated that the phosphorylated residue was confirmed as Ser-71 by phospho-amino analysis giving the impression that they performed the phospho-amino acid analysis. I am the person who discovered that I-2 was phosphorylated on Serine 71.

[1. I challenge both Hugh C. Hemmings, Jr. and Jimcy Platholi to obtain brain tissue from a freshly killed pig, prepare the brain homogenate, prepare the various chromatographic columns and purify PP-1I from the various chromatographic steps in the cold room. I am quite confident that they will not be able to do so. That is why they resorted to stealing my data, fabricating data and falsifying data.

2. I challenge both Hugh C. Hemmings, Jr. and Jimcy Platholi to produce the raw data with respect the preparation of ^{32}P-labeled phosphorylase a, the specific radioactivity of

the ^{32}-ATP used to phosphorylate phosphorylase b, the specific radioactivity of ^{32}P-labeled phosphorylase a used to assay PP-1I during its purification.

3. I challenge both Hugh C. Hemmings, Jr. and Jimcy Platholi to produce the raw data with respect to the calibration of the gel filtration column used to analyze the molecular mass of purified PP-1I. I also challenge both Hugh C. Hemmings, Jr. and Jimcy Platholi to produce the raw data with respect the preparation of ^{32}P-labeled phosphorylase a, the specific radioactivity of the ^{32}-ATP used to phosphorylate phosphorylase b, the specific radioactivity of ^{32}P-labeled phosphorylase a used to assay PP-1I described in Figure 1

4. I challenge both Hugh C. Hemmings, Jr. and Jimcy Platholi to produce the raw data with respect to the calibration of the gel filtration column used to analyze the molecular mass of purified PP-1I. I also challenge both Hugh C. Hemmings, Jr. and Jimcy Platholi to produce the raw data with respect the preparation of ^{32}P-labeled phosphorylase a, the specific radioactivity of the ^{32}-ATP used to phosphorylate phosphorylase b, the specific radioactivity of ^{32}P-labeled phosphorylase a used to assay PP-1I described in Figure 2

5. I challenge both Hugh C. Hemmings, Jr. and Jimcy Platholi to produce the raw data for the calculation of the data that showed that I-2 was phosphorylated on Seine 71].

Data Falsification and Data Fabrication:

A. The Data in Figure 3A is falsified to show phosphorylation of I-2 by PFTK1 Protein Kinase occurs at the same rate as C-TAK-1. Even the control shows phosphorylation of I-2 by PFTK1 Protein Kinase.

[I challenge Hugh C. Hemmings, Jr. and Jimcy Platholi to produce the original data in an original laboratory notebook in which it is described that the Control phosphorylation and the PTFK1 Protein Kinase phosphorylation were performed at the same time, what the specific radioactivity of the ^{32}P-ATP was and how long was the autoradiography].

B. In the paper, the authors including Hugh C. Hemmings, Jr. and Jimcy Platholi showed that reconstituted PP-1I was activated almost 5.5 fold by GSK-3β in Figure 1B . However, under the same condition, reconstituted PP-1I was activated almost 30 fold by reconstituted PP-1I in Figure 1C. Both results cannot be correct. One is fabricated.

[I challenge Hugh C. Hemmings, Jr. and Jimcy Platholi to produce the original data in an original laboratory notebook in which it is described the results of the phosphorylation and activation of reconstituted PP-1I by GSK-3β that is presented in Figure 3B and 3C]

C. The authors including Hugh C. Hemmings, Jr. and Jimcy Platholi stated in the paper that PFTK1 protein kinase had no effect on the activity of reconstituted PP-1I or on the phosphorylation and activation of reconstituted PP-1I by GSK-3β and presents Figure 3C as evidence. However Figure 3C is most probably fabricated as described above. In Figure 3C, the authors including Hugh C. Hemmings, Jr. and Jimcy Platholi did not do the experiment to show that PFTK1 protein kinase had no effect on the phosphorylation and activation of reconstituted PP-1I by GSK-3β.

Figure 3C actually shows that PFTK1 protein kinase can cause the activation of reconstituted PP-1I in the presence of Mg-ATP if the result is re-plotted with the scale used in Figure 1B. However, it is clear that there are major problems with Figure 3C.
[I challenge Hugh C. Hemmings, Jr. and Jimcy Platholi to produce the original data in an original laboratory notebook in which it is described the results of the phosphorylation and activation of reconstituted PP-1I by GSK-3β and C-TAK-1 and PFTK1 protein kinase that is presented in Figure 3B and 3C.]

D. In the paper, the authors including Hugh C. Hemmings, Jr. and Jimcy Platholi claim that phosphorylation of reconstituted by PFTK1 Protein Kinase potentiates the activation of reconstituted PP-1I by GSK-3β. That experiment was never done (See Figure 3C).

The author,s including Hugh C. Hemmings, Jr., Jr. Jimcy Plathol never performed the experiment that showed that PFTK1 Protein Kinase can phosphorylate reconstituted PP-

1I. This is clear Data Falsification. The title to Figure 3 states that Reconstituted PP-1I is not activated by C-TAK1 or PFTK1 Protein Kinase. Yet they did not do the experiments that show phosphorylation of reconstituted PP-1I by C-TAK-1 or PFTK1 Protein Kinase. This is clear Data falsification.

[I challenge Hugh C. Hemmings, Jr. and Jimcy Platholi to produce the original data in an original laboratory notebook in which it is described the results of the phosphorylation and activation of reconstituted PP-1I by GSK-3β and C-TAK-1 and PFTK1 protein kinase that is presented in Figure 3B and 3C.]

P. There is extensive data fabrication and data falsification with respect to Figure 6.
In Figure 6A, the authors including Hugh C. Hemmings, Jr., and Jimcy Platholi show and state that only 0.01 mole of WT I-2 is phosphorylated by PFTK1 Protein Kinase and that under similar conditions CKI and CKII (casein kinase I and casein kinase II) phosphorylated WT I-2 to a similar extent or less (See Figure 6C) implying that CKI and CKII also phosphorylated WT with a stoichiometry of only 0.01 mole/mol or less. This data is in stark contradiction to published data from reputable laboratories that are experts in the field [See the papers Synergistic Phosphorylation and Activation of ATP-Mg-dependent Phosphoprotein Phosphatase by FA/GSK-3 and Casein Kinase I1 (PC0.7) by Anna A. De Paoli-Roach [J. Biol. Chem., Vol 259, pp12144-12144 (1984)] and Analysis of the in vivo phosphorylation state of protein phosphatase inhibitor-2 from rabbit skeletal muscle by fast-atom bombardment mass spectrometry by CFB Holmes et al, [Biochimica et BiophysicaActa (BBA) - Molecular Cell Research, Vol 929, pp208-219 (1987)].

It is well established that Casein Kinase II phosphorylates I-2 with a stoichiometry of more than 1 mol/mol. and up to 2 mol/mol).

[I challenge Drs Hugh C. Hemmings, Jr., Jr. Jimcy Platholi and Paul Heerdt to produce the original data in an original laboratory notebook in which it is shown that CKI and

CKII phosphorylated WT I-2 with a stoichiometry of only 0.01 mol/mol or less. The Data is fabricated].

In Figure 6D, Drs Hugh C. Hemmings, Jr., Jr. Jimcy Platholi and Paul Heerdt showed the phosphorylation of I-2 by PFTK1 Protein Kinase in the presence of CK1 Inhibitor and CK2 Inhibitor. The experiments appear to have been done at the same time. However, in Figure 6C, the phosphorylation of I-2 (wild type) and I-2(S86A mutant) by PFTK1 Protein Kinase and CKI and CKII were not done at the same time. There is clear Data Falsification.

Moreover, the authors including Hugh C. Hemmings, Jr., and Jimcy Platholi reported in Figure 5A that I-2 is phosphorylated by PFTK1 Protein Kinase with a stoichiometry of around 0.01 mol/mol. This is a clearly substandard experiment. The authors should have done the phosphorylation of I-2 by PFTK1 Protein Kinase as with the phosphorylation of I-2 by C-TAK1 described in Figure 4. The reason they did not do it or did not report that they tried to do it is because recombinant PFTK1 protein kinase which the authors used was either inactive or had very low specific activity. The data presented in Figure 6 is therefore dubious.

Because the Data presented in Figure 6A and 6C is either fabricated and falsified, the Data presented in Figure 6B and 6D are also toxic as they are compared to WT I-2 being phosphorylated with a stoichiometry of 0.01 mol/mol or less. A thorough investigation of the original data in an original laboratory notebook will show whether the data presented in Figure 6B and 6D were actually performed and whether the I-2 mutants were actually made and characterized.

It is clear that the authors including Hugh C. Hemmings, Jr. and Jimcy Platholi are not experts in the field. Had they been experts, they would have known that it is well established that Casein Kinase II phosphorylates I-2 with a stoichiometry of more than 1 mol/mol. and up to 2 mol/mol. Moreover, they would not have fabricated the data in Figure 6A and 6C to suit their impossible hypothesis and conclusion.

The title of the paper which states that Brain Protein Phosphatase-1 Complex has two opposing kinases is false as the authors did not do the requisite experiments but stole data, fabricated data and falsified data to construct an impossible conclusion.

Indeed, Figure 6C shows that recombinant I-2 is phosphorylated by PFTK1 Protein Kinase with a stoichiometry of only 0.01 mil/mol. If the data is true and has been performed, with such a low stoichiometry, one would hardly observe any effect for the simple reason that the enzyme preparation was inactive or had very low specific activity.

[I challenge Hugh C. Hemmings, Jr. and Jimcy Platholi to produce the original data in an original laboratory notebook that show that the specific activity of PFTK1 Protein Kinase was determined.]

After reading the above, one must ask the question: why would Hugh C. Hemmings, Jr. and Jimcy Platholi resort to Theft of Data, Data Fabrication and Data falsification. Was it out of desperation. In 2014 after five years of collecting NIH funding illegitimately in the amount of more than $ 1,500000 for themselves and more than $600,000 as indirect cost for Weill Cornell Medical College, Hugh C. Hemmings, Jr and Jimcy Platholi could not come up with a single Scientific Article because they did not know how to and could not purify PP-1I holoenzyme from freshly killed pig brain. They could never show the phosphorylation of I-2 and reconstituted PP-1I by PFTK1 Protein Kinase at significant level. If they could, they would have been able to determine the phosphorylation site by Mass Spectrometry as with the phosphorylation of I-2 by C-TAK1 (performed by me). The NIH Research Grant (stolen by Hugh C. Hemmings, Jr. and Jimcy Platholi) which I conceived, performed and generated the preliminary data, wrote and submitted called for the study of PP-1I holoenzyme in cell death control. None of that work was performed for the simple reason that Hugh C. Hemmings, Jr and Jimcy Platholi do not have any clue as to what it entails. Basically, they wasted tax payer's money and collected payment from the NIH under false pretense, a clear violation of the False Claim Act and the Mail and Wire Fraud Statutes.

B. Evidence of Data Fabrication and Data Falsification in the Scientific Article "Synthetic Peptide Analogs of DARPP-32 (Mr 32,000 Dopamine- and cAMP-regulated Phosphoprotein), an Inhibitor of Protein Phosphatase-1" authored by Hugh C. Hemmings, Jr., Angus C. Nairn, James I. Elliot, and Paul Greengard and published in J. Biol. Chem. (1990) Vol. 265, pp20369-20376.

In the Scientific Article [Synthetic Peptide Analogs of DARPP-32 (Mr 32,000 Dopamine- and cAMP-regulated Phosphoprotein), an Inhibitor of Protein Phosphatase-1 (1990) Vol. 265, pp20369-20376], Hugh C. Hemmings, Jr. and Angus Nairn reported in Table III that their purified PP-1_C and $PP2A_C$ had specific activities of 84 units/mg or 84 nmol/min/mg and 360 units/mg or 360 nmol/min/mg respectively using ^{32}P-labeled phosphorylase a as substrate. It is quite laughable and impossible for PP-1_C and PP-$2A_C$ to have specific activities of 84 units/mg and 360 units/mg respectively using ^{32}P-labeled phosphorylase a as substrate [See the Scientific Articles, Characterization of a Reconstituted Mg-ATP-Dependent Protein Phosphatase by Therese J. Resink et al., Eur. J. Biochem. (1983) Vol. 133 pp455-461, The Catalytic Subunits of Protein Phosphatase-1 and Protein Phosphatase-2A are Distinct Gene Products by H.Y.L. Tung et al., Eur. J. Biochem. (1984) Vol 138, pp635-641, and Isolation and Characterization of Rabbit Skeletal Muscle Protein Phosphatases C-I and C-11" by Steven R. Silberman et al., J. Biol. Chem. (1984) Vol. 259, pp 2913-2922.]. In Table II, Hugh C. Hemmings, Jr. and Angus Nairn reported that the relative activity of PP-$2A_C$ was 120%, 150% and 40 % when Phospho-D32-(8-48), Phospho-D32-(8-38) and Phospho-D32-[Ser34]8-38 were used as substrates respectively. In Table III of the same Scientific Article, Hugh C. Hemmings, Jr. and Angus Nairn reported the specific activity of PP-$2A_C$ was as 360 units /mg or 360 nmol/min/mg when ^{32}P-Phosphorylase a was used as substrate and 1100 units/mg or 1100 nmol/min/mg when Phospho-D32-([Ser34] 8-38 was used as substrate. Hugh C. Hemmings, Jr. and Angus Nairn did not report the specific activities of PP-2Ac when Phospho-DARPP-21 and Phospho-D32(8-38) because they claimed that they could not obtain a linear Lineweaver-Burk plot. {It is well documented that one can obtain Vmax value without a Lineweaver-Burk plot. It is elementary Enzyme Kinetics that every students of Enzymology should know). The results reported in Table II and Table

III show that there has been data fabrication because results in Table II contradict results reported in Table III.

In Table II, Hugh C. Hemmings, Jr. and Angus Nairn reported the relative activity of PP-$2A_C$ as 100% and relative activities of PP-$2A_C$ as 120 %, 150% and 40% when Phospho-D32-(8-48), Phospho-D32-(8-38) and Phospho-D32-([Ser34]8-38) were used respectively. The results mean that the specific activities of PP-2A were 360 units/mg or nmol/min/mg when 32P-labeled phosphorylase a was the substrate, ~432 units or ~ nmol/min/mg (i.e 120% of 360) when Phospho-D32-(8-48) was the substrate, ~540 units/mg or ~540 nmol/min/mg (i.e 150% of 360) when Phospho-D32-(8-38) was the substrate, and 144 units/mg or 144 nmol/min/mg (i.e 40% of 360) when Phospho-D32-([Ser34]8-38) was the substrate.

Yet in Table III, Hugh C. Hemmings, Jr. and Angus Nairn reported that they could not determine the Vmax value for PP-2AC when Phospho-DARPP-32 and when Phospho-D32-(8-38) were the substrates because they claimed that they could not obtain a liner Lineweaver-Burk plot. Any students of Enzymology who has done elementary Enzyme Kinetics will tell you that one does not need to have a Lineweaver-Burk plot to obtain Vmax value (i.e Specific Activity). In Table III, Hugh C. Hemmings, Jr. and Angus Nairn reported that the specific activity of PP-2AC was 1100 units/mg or 1100 nmol/min/mg when Phospho-D32-([Ser34]8-38) was the substrate in stark contradiction to the reported figure of 144 units/mg or 144 nmol/min/mg in Table II. Both results cannot be correct. Either the results in Table II are fabricated or the results in Table III are fabricated. The results in Table II are most likely fabricated because in Table III, Hugh C. Hemmings, Jr. and Angus Nairn stated that they could not determine the Vmax value for PP-2AC when Phospho-DARPP32 and Phospho-D32-(8-38) were used as substrates. If they could not determine the Vmax values, how did they determine the relative activities of PP-2AC when Phospho-DARPP32 and Phospho-D32-(8-38) were the substrates as described in Table II. Moreover, Hugh C. Hemmings, Jr. and Angus Nairn reported in Table II that the stoichiometry of phosphorylation of phosphorylase a is 1.1. The idea that one can phosphorylate phosphorylase b to form phosphorylase a with a stoichiometry of 1.1 mol

of ^{32}P-labeled phosphate per mol of phosphorylase a is just laughable, impossible and against the laws of nature [If it is true that Hugh C. Hemmings, Jr. and Angus Nairn can phosphorylate Phosphorylase b with Phosphorylase Kinase with a stoichiometry of 1.1, it would mean that the Specific Radioactivity of their prepared ^{32}P-labeled Phosphorylase a would be increased by ~10% [i.e we are talking of over 50000 - 100000 cpm in excess of what the value should be]. Simple arithmetic states that there is something very fishy here. .

Hugh C. Hemmings, Jr. and Angus Nairn reported in the Experimental Procedures Section of the Scientific Article that in each of their Assay for Inhibition of Protein Phosphatase-1 Activity, they used 0.3 unit/ml of PP-1$_C$ per Assay of 30 µl (i.e the total amount of PP-1$_C$ used in each assay was .009 unit.) They defined one unit of PP-1$_C$ as the amount of enzyme that catalyses the dephosphorylation of 1 µmol ^{32}P-labeled phosphorylase a. The idea that one can assay .009 unit of PP-1$_C$ and still be in the linear range is quite laughable, impossible and against the laws of nature. If they were using .009 unit of PP-1$_C$, it would mean that they were counting up to 4,500000 to 9,000000 cpm in each assay which is laughable, impossible and against the laws of nature because

Hugh C. Hemmings, Jr. and Angus Nairn stated in the Experimental Procedures Section that they prepared ^{32}P-labeled Phosphorylase a that had a specific radioactivity of 5-10 x 105 cpm/nmol or 5000-10000 x 105 cpm/µmol and they used 1mg/ml of ^{32}P-labeled phosphorylase a in the assay of 30 µl (i.e 5 nmol/ml of 32P-labeled Phosphorylase a in the assay of 30 µl or 0.3 nmol of ^{32}P-labeled phosphorylase in the assay of 30 µl. Meaning that they only had a maximum of 150000 to 300000 cpm to start with. If they were using 0.009 unit of PP-1$_C$ (i.e .009 umol or 9 nmol ^{32}P-labeled Pi released per min) in each assay, it would mean that at 10% of total dephosphorylation (that is what one usually aims for when one is assaying for inhibitors of PP-1C), there would be ~450000 to ~9000000 cpm released per Assay. Since they reported that their Assay was performed for 10 minutes, there would be ~4500000 to 9000000 cpm released per Assay.

The above indicates that they were not assaying PP-1_C in the linear range but most importantly that they had fabricated the data. Even at 1% of total dephosphorylation, there would be ~450000 to ~900000 cpm released. Simple arithmetic says that the above scenario is impossible and against the laws of nature.

Because of the discrepancies in the reported specific activities of PP-1_C and PP-$2A_C$, and anomaly in the specific radioactivity of ^{32}P-labeled Phosphorylase a used to assay PP-1_C in the presence of Phospho-DARPP-32 and Phospho-D32-peptides, all the reported results in the paper with respect to the inhibition of PP-1_C by Phospho-DARPP-32 and Phospho-D32-peptides are suspect and toxic.

Further, all the studies of the Phosphorylation of Phospho-DARPP-32 and Phospho-D32-peptides may also be suspect and toxic. Investigative critiques with access to the raw data will be necessary to determine if there has been Data Fabrication and Data Falsification with respect to the studies of the Phosphorylation of Phospho-DARPP-32 and Phospho-D32-peptides as well.

The actions of Hugh C. Hemmings, Jr. and Angus Nairn constitute a clear violation of Scientific Ethics through Data Fabrication and Data Falsification. The actions constitute Scientific Misconduct through Data Fabrication and Data Falsification. Although, Paul Greengard is an author in the above paper, It is unlikely that Paul Greengard would know about the actions because Paul Greengard is an "Arm Chair" scientist, had moved away from the laboratory bench long time ago and is not a student or expert of Enzymology and Enzyme Kinetics.

C. Evidence of Dishonest Scientific Report in the Scientific Article, "Regulation of Protein Phosphatase Inhibitor-1 by Cyclin-dependent Kinase 5" by Chan Nguyen , Akinori Nishi , Janice W. Kansy , Joseph Fernandez , Kanehiro Hayashi , Frank Gillardon , Hugh C. Hemmings, Jr., Angus C. Nairn, and James A. Bibb. [J. Biol. Chem. (2006) Vol. 282, pp 16511-16520.]

On or around November 2005, Hugh C. Hemmings, Jr. and James Bibb came to me to discuss about a collaboration. They did not know how to purify the enzyme protein phosphatase-1_C (PP-1_C) that they needed to perform certain experiments with and that they planned to include in a paper to be submitted to the Journal of Biological Chemistry. I agreed on the principle that I will be a collaborator and a co-author of the paper. Specifically, I would personally purify the enzyme protein phosphatase-1_C (PP-1_C) and teach James Bibb's student, Chan Nguyen on how to assay the enzyme using ^{32}P-labeled phosphorylase a as substrate. I was surprised that they could not do that themselves in that the procedures are published in several journals, including the European Journal of Biochemistry and Methods in Enzymology. When you yourself work at the bench and you follow the rules of Scientific Ethics, it is not possible to publish too many Scientific Papers. Every paper counts. So, I worked diligently by going to the slaughterhouse in Queens (NYC), New York to obtain muscle tissue from freshly killed rabbits and brought it back to the laboratory and purified protein phosphatase-1_C (PP-1_C) [according to Tung et al. Eur. J. Biochem. (1984) Vol. 138, pp635-641.] in the cold for five days. I also prepared ^{32}P-labeled Phosphorylase a in order to be able to assay for purified protein phosphatase-1 (PP-1C).

After teaching James Bibb's student, Chan Nguyen on how to assay for protein phosphatase-1_C(PP-1_C) that I spent four days purifying in the cold room purifying using ^{32}P-labeled Phosphorylase a as substrate that I prepared to the detriment of my health [Preparing ^{32}P-labeled phosphorylase a may look easy on paper. However, it involved not only expertise but also the knowledge to dispose of about mCi of ^{32}P-labeled ATP without contaminating everything in the laboratory, including centrifuges, pipettes, etc., I handed a large amount of purified protein phosphatase-1_C (PP-1_C) to James Bibb's student hoping that my contribution will be recognized as a co-author. James Bibb and his student, published the Scientific Article in the Journal of Biological Chemistry [Regulation of Protein Phosphatase Inhibitor-1 by Cyclin-dependent Kinase 5 by Chan Nguyen et al. (2006) J. Biol. Chem. Vol. 282, pp 16511-16520.

To my surprise and disgust, they did not include me as an author but they included Hugh C. Hemmings, Jr. and Angus Nairn as co-authors when they did not do "shit" with respect to the paper. James Bibb acknowledged me in the Acknowledgment Section with out my permission. Even more disgusting is the fact that neither Hugh C. Hemmings, Jr. nor James Bibb had the courage to tell me that they decided not to include me as an author.

The action of Hugh C. Hemmings, Jr. and James Bibb and his student, Chan Nguyen constitutes Dishonest Scientific Reporting and violates Scientific Ethics. Now. why would Hugh C. Hemmings, Jr. and James Bibb and his student, Chan Nguyen thought that they could get away with their dishonesty. They knew or had reason to know that the whole world will know about their dishonest practice after the publication of their paper.

EXHIBIT F

Weill Cornell Medicine

Thomas H. Blair, JD
Research Integrity Officer
Senior Director, Administration

Dr. H.Y. Lim Tung
31-70 Crescent Street
Astoria, NY 11106

February 25, 2018
Sent via email

Dear Dr. Tung,

I am writing to advise you that I have completed my assessment of your scientific misconduct complaints dated December 28th, 2016, which were emailed to Dean Augustine Choi. My assessment included:

- Interview with you, as claimant.
- Multiple interviews with respondents, Drs. Hemmings, Platholi and Heerdt.
- Review of the lab notebooks and other data created in the course of experimentation that was used to support the conclusions put forth in the August 22, 2014 paper published in the Journal of Biological Chemistry.
- An independent review of the journal paper in question by a senior scientist at Weill Cornell.
- An independent review of the materials by the Acting Deciding Official appointed by Dean Choi to handle this case.

After this review, pursuant to WCM policy, I have determined that a panel inquiry is not warranted in this case and have recommended such to WCM's Acting Deciding Official. The Acting Deciding Official, in this matter, independently reviewed the material and has accepted my recommendation. As such, we will be closing our review of your complaints in this matter. I have discussed my findings with the National Institute of Health's Office of Research Integrity case officer assigned to this incident.

As previously mentioned, my role, as RIO is limited to a review of the allegations of scientific misconduct. Your other concerns have been forwarded to Deputy University Counsel, James Kahn, copied above. You should direct any inquiries on those matters to him.

Best,

Thomas H. Blair

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END